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4-562

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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: MARK BERCH Examiner #: 59193 Date: 4/13/02
Art Unit: 1624 Phone Number: 2-0663 Serial Number: 10511537D
Location (Bldg/Room#): 5C01 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following: ME

Title of Invention: _____

Inventors (please provide full names): _____

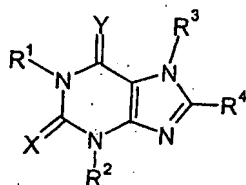
Earliest Priority Date: _____

Search # 4

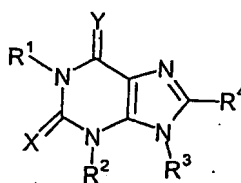
Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



(Ia)



(Ib)

X = S Y = O

4, A', R1, R3, R4 = H/CH3

R2 = (A' C A')n - O - J

J = CH3/C2H5

20070412-10511537-244

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Searcher: books

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 4-12-07

Searcher Prep & Review Time: 20

Online Time: 11

Type of Search

____ NA Sequence (#)

____ AA Sequence (#)

2 Structure (#)

____ Bibliographic

____ Litigation

____ Fulltext

____ Other

Vendors and cost where applicable

55 STN _____ Dialog

____ Questel/Orbit _____ Lexis/Nexis

____ Westlaw _____ WWW/Internet

____ In-house sequence systems

____ Commercial _____ Oligomer _____ Score/Length
____ Interference _____ SPDI _____ Encode/Transl
____ Other (specify)

=> fil reg; d stat que 127; fil cap1; s 127
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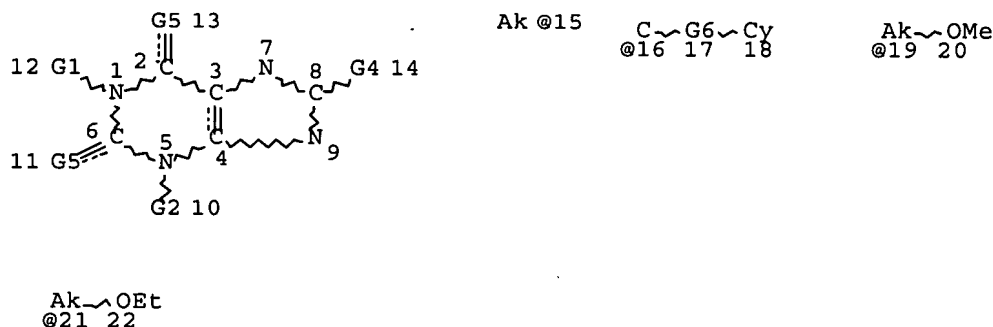
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experimental property data in the original document. For information
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L1 STR

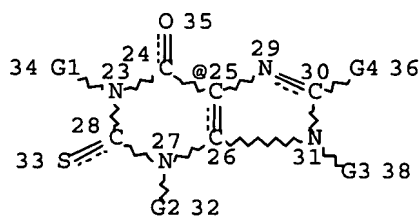
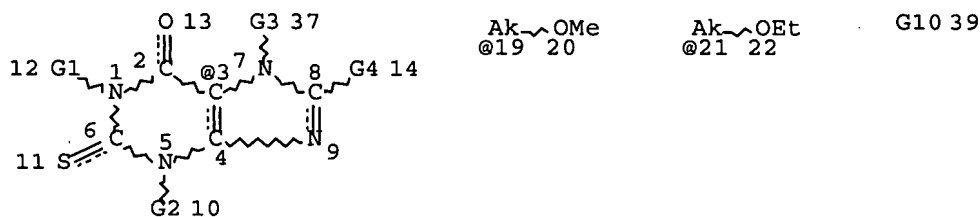


VAR G1=H/15
VAR G2=16/15/OME/OET/19/21
VAR G4=H/AK
VAR G5=O/S
REP G6=(0-5) C
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 15
CONNECT IS E2 RC AT 19
CONNECT IS E2 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

L4 17287 SEA FILE=REGISTRY SSS FUL L1
L24 STR



VAR G1=H/ME
VAR G2=OME/OET/19/21
VAR G3=H/ME
VAR G4=H/ME
VAR G10=3/25

NODE ATTRIBUTES:

CONNECT IS E2 RC AT 19
CONNECT IS E2 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE

L27 2 SEA FILE=REGISTRY SUB=L4 SSS FUL L24

100.0% PROCESSED 229 ITERATIONS
SEARCH TIME: 00.00.01

2 ANSWERS

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FILE COVERS 1907 - 12 Apr 2007 VOL 146 ISS 16
FILE LAST UPDATED: 11 Apr 2007 (20070411/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L28 1 L27

=> d ibib ed abs hitstr l28; fil hom

Wink

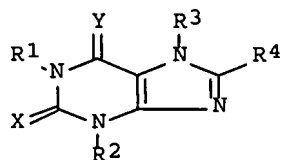
L28 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:855927 CAPLUS Full-text
DOCUMENT NUMBER: 139:350580
TITLE: Preparation of xanthinethione derivatives as
myeloperoxidase inhibitors
INVENTOR(S): Hanson, Sverker; Nordvall, Gunnar; Tiden, Anna-Karin
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003089430 | A1 | 20031030 | WO 2003-SE617 | 20030415 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2480452 | A1 | 20031030 | CA 2003-2480452 | 20030415 |
| AU 2003224548 | A1 | 20031103 | AU 2003-224548 | 20030415 |
| EP 1499613 | A1 | 20050126 | EP 2003-721211 | 20030415 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003009012 | A | 20050201 | BR 2003-9012 | 20030415 |
| CN 1646531 | A | 20050727 | CN 2003-808355 | 20030415 |
| JP 2005526836 | T | 20050908 | JP 2003-586151 | 20030415 |
| NZ 535406 | A | 20060831 | NZ 2003-535406 | 20030415 |
| ZA 2004007815 | A | 20051004 | ZA 2004-7815 | 20040928 |
| US 2005234036 | A1 | 20051020 | US 2004-511537 | 20041015 |
| NO 2004004998 | A | 20050118 | NO 2004-4998 | 20041117 |
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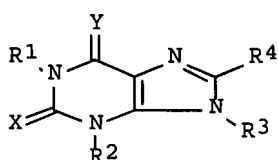
SE 2002-2239
WO 2003-SE617

A 20020717
W 20030415

OTHER SOURCE(S): MARPAT 139:350580
ED Entered STN: 31 Oct 2003
GI



I



II

AB Xanthinethiones I and II [one of X and Y = S, the other = O, S; R1, R3, R4 = H, alkyl; R2 = H, (un)substituted alkyl] were prepared for use as myeloperoxidase (MPO) inhibitors in the treatment of neuroinflammatory disorders. Thus, Me2CHCH2NHCSNH2 was cyclized with NCCH2CO2Et to give 6-amino-1-isobutyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one which was nitrosated, reduced to the 5,6-diamine, and cyclized with HCO2H to give II [R1, R3, R4 = H, R2 = CH2CHMe2, X = S, Y = O]. This compound had IC50 for inhibition of MPO of 0.87 μ M.

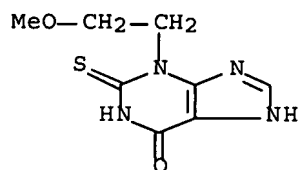
IT 618913-25-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

RN 618913-25-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(2-methoxyethyl)-2-thioxo- (9CI) (CA INDEX NAME)



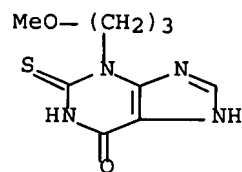
IT 618913-21-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

RN 618913-21-6 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(3-methoxypropyl)-2-thioxo- (9CI) (CA INDEX NAME)

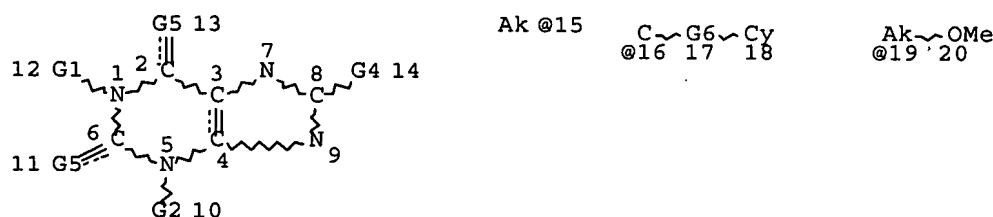


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

FILE 'HOME' ENTERED AT 16:47:03 ON 12 APR 2007

SEARCH HISTORY

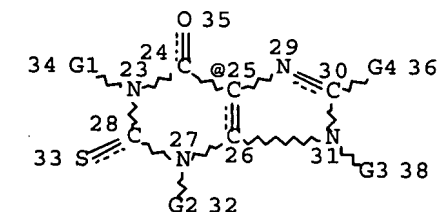
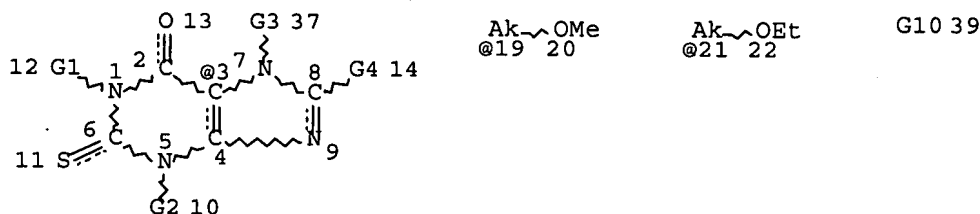
=> d stat que l27; d his nofile
L1 STR



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VAR G2=16/15/OME/OET/19/21
VAR G4=H/AK
VAR G5=O/S
REP G6=(0-5) C
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 15
CONNECT IS E2 RC AT 19
CONNECT IS E2 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L4 17287 SEA FILE=REGISTRY SSS FUL L1
L24 STR



VAR G1=H/ME

VAR G2=OME/OET/19/21
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VAR G10=3/25
NODE ATTRIBUTES:
CONNECT IS E2 RC AT 19
CONNECT IS E2 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE
L27 2 SEA FILE=REGISTRY SUB=L4 SSS FUL L24

100.0% PROCESSED 229 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

(FILE 'HOME' ENTERED AT 16:04:30 ON 12 APR 2007)

FILE 'REGISTRY' ENTERED AT 16:04:37 ON 12 APR 2007

L1 STR
L2 50 SEA SSS SAM L1
L3 115605 SEA SSS FUL L1 EXTEND
L4 17287 SEA SSS FUL L1
SAVE TEMP L4 BER537FULL/A
L5 STR L1
L6 1 SEA SUB=L4 SSS SAM L5
D SCAN
L7 229 SEA SUB=L4 SSS FUL L5 EXTEND
L8 17 SEA SUB=L4 SSS FUL L5
SAVE TEMP L8 BER537FULA/A

FILE 'REGISTRY' ENTERED AT 16:17:11 ON 12 APR 2007
D STAT QUE L8

FILE 'CAPLUS' ENTERED AT 16:17:15 ON 12 APR 2007

L9 8 SEA ABB=ON L8
D IBIB ED ABS HITSTR 1-8

FILE 'HOME' ENTERED AT 16:17:29 ON 12 APR 2007
D STAT QUE L8
D COST

FILE 'REGISTRY' ENTERED AT 16:18:23 ON 12 APR 2007

L10 STR L5
L11 1 SEA SUB=L4 SSS SAM L10
D SCAN
L12 52 SEA SUB=L4 SSS FUL L10 EXTEND
L13 6 SEA SUB=L4 SSS FUL L10
SAVE TEMP L13 BER537FULB/A

FILE 'REGISTRY' ENTERED AT 16:27:53 ON 12 APR 2007

D STAT QUE L13

L14 FILE 'CAPLUS' ENTERED AT 16:27:53 ON 12 APR 2007
4 SEA ABB=ON L13
D IBIB ED ABS HITSTR L14 1-4

FILE 'HOME' ENTERED AT 16:28:06 ON 12 APR 2007
D STAT QUE L13
D COST

FILE 'STNGUIDE' ENTERED AT 16:28:33 ON 12 APR 2007

L15 FILE 'REGISTRY' ENTERED AT 16:30:19 ON 12 APR 2007
STR L5
L16 STR L10
L17 3 SEA SUB=L4 SSS SAM L16
D SCAN
L18 263 SEA SUB=L4 SSS FUL L16 EXTEND
L19 23 SEA SUB=L4 SSS FUL L16
SAVE TEMP L19 BER537FULC/A
L20 ANALYZE L19 1- LC : 7 TERMS
D

FILE 'REGISTRY' ENTERED AT 16:37:19 ON 12 APR 2007
D STAT QUE L19

L21 FILE 'CAPLUS' ENTERED AT 16:37:19 ON 12 APR 2007
18 SEA ABB=ON L19

L22 FILE 'CAOLD' ENTERED AT 16:37:20 ON 12 APR 2007
4 SEA ABB=ON L19

L23 FILE 'CAPLUS, CAOLD' ENTERED AT 16:37:27 ON 12 APR 2007
22 DUP REM L21 L22 (0 DUPLICATES REMOVED)
ANSWERS '1-18' FROM FILE CAPLUS
ANSWERS '19-22' FROM FILE CAOLD
D IBIB ED ABS HITSTR 1-18
D IALL HITSTR 19-22

FILE 'HOME' ENTERED AT 16:38:01 ON 12 APR 2007
D STAT QUE L19
D SAVED

FILE 'STNGUIDE' ENTERED AT 16:38:42 ON 12 APR 2007
D COST

L24 FILE 'REGISTRY' ENTERED AT 16:39:32 ON 12 APR 2007
STR L1\

FILE 'STNGUIDE' ENTERED AT 16:42:39 ON 12 APR 2007
D L24

L25 FILE 'REGISTRY' ENTERED AT 16:45:29 ON 12 APR 2007
1 SEA SUB=L4 SSS SAM L24
D SCAN
L26 229 SEA SUB=L4 SSS FUL L24 EXTEND
L27 2 SEA SUB=L4 SSS FUL L24
SAVE TEMP L27 BER537FULD/A
D LC 1-2

FILE 'REGISTRY' ENTERED AT 16:46:52 ON 12 APR 2007
D STAT QUE L27

FILE 'CAPLUS' ENTERED AT 16:46:53 ON 12 APR 2007
L28 1 SEA ABB=ON L27
D IBIB ED ABS HITSTR L28

FILE 'HOME' ENTERED AT 16:47:03 ON 12 APR 2007
D STAT QUE L27

=>

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Requester's Full Name: MARK BERCH Examiner #: 59193 Date: 4/13/07
 Art Unit: 1624 Phone Number: 2-0663 Serial Number: 10511537.C
 Location (Bldg/Room#): 5C01 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following: ME

Title of Invention: _____

Inventors (please provide full names): _____

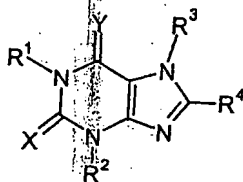
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Search #06

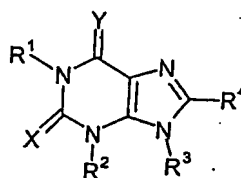
Search Topic:

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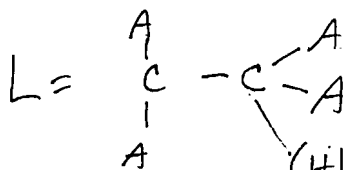
(Ia)



(Ib)

All A = H | CH₃

X = O Y = S

(H | CH₃ | C₂H₅ | C₃H₇)R₄ = H | CH₃ | C₂H₅R₃ = A

non-1-

R₁ = H | CH₃ | ~~C₂H₅~~ LR₂ = L

20070412-10511537-str3

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Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 4-12-07Searcher Prep & Review Time: 20Online Time: 11

Type of Search

____ NA Sequence (#)

____ AA Sequence (#)

____ 2 Structure (#)

____ Bibliographic

____ Litigation

____ Fulltext

____ Other

Vendors and cost where applicable

1166 STN _____ Dialog

____ Questel/Orbit _____ Lexis/Nexis

____ Westlaw _____ WWW/Internet

____ In-house sequence systems

____ Commercial _____ Oligomer _____ Score/Length
 ____ Interference _____ SPDI _____ Encode/Transl
 ____ Other (specify)

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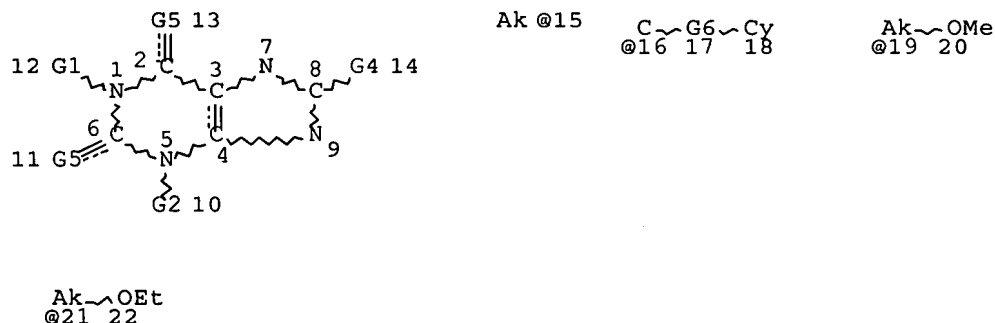
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L1 STR



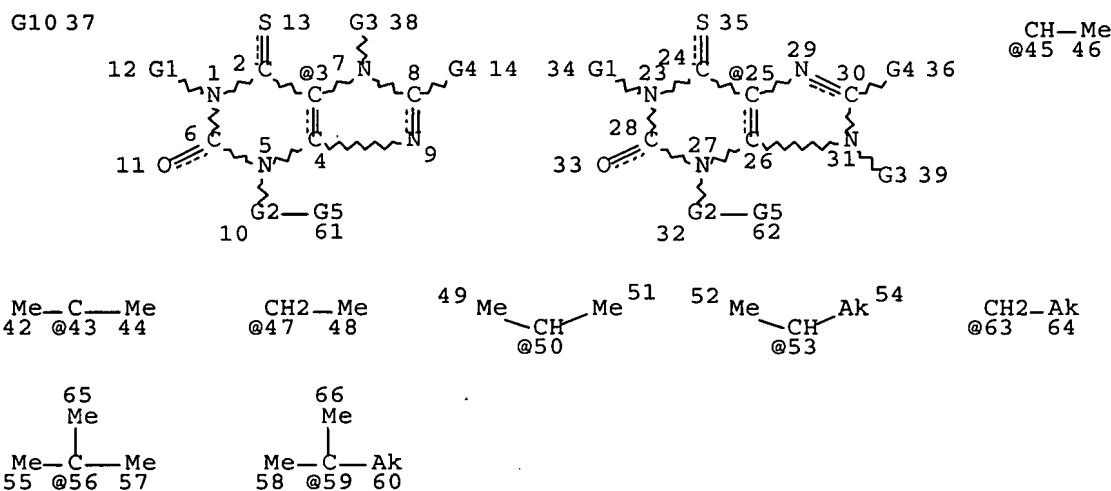
VAR G1=H/15
VAR G2=16/15/OME/OET/19/21
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REP G6=(0-5) C
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 15
CONNECT IS E2 RC AT 19
CONNECT IS E2 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

L4 17287 SEA FILE=REGISTRY SSS FUL L1

L16 STR



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VAR G2=CH2/45/43

VAR G3=H/ME

VAR G4=H/ME/ET

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VAR G10=3/25

NODE ATTRIBUTES:

CONNECT IS E2 RC AT 54

CONNECT IS E2 RC AT 60

CONNECT IS E2 RC AT 64

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS M2-X3 C AT 54

ECOUNT IS M2-X3 C AT 60

ECOUNT IS M2-X3 C AT 64

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE

L19 23 SEA FILE=REGISTRY SUB=L4 SSS FUL L16

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SEARCH TIME: 00.00.01

23 ANSWERS

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FILE LAST UPDATED: 11 Apr 2007 (20070411/ED)

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L21 18 L19

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L22 4 L19

=> dup rem l21,l22
DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
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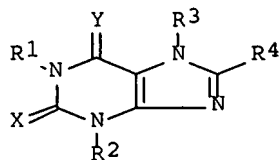
FILE 'CAOLD' ENTERED AT 16:37:27 ON 12 APR 2007
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PROCESSING COMPLETED FOR L21
PROCESSING COMPLETED FOR L22
L23 22 DUP REM L21 L22 (0 DUPLICATES REMOVED)
ANSWERS '1-18' FROM FILE CAPLUS
ANSWERS '19-22' FROM FILE CAOLD

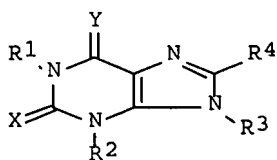
=> d ibib ed abs hitstr 1-18; d iall hitstr 19-22; fil hom

L23 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:855927 CAPLUS Full-text
DOCUMENT NUMBER: 139:350580
TITLE: Preparation of xanthinethione derivatives as
myeloperoxidase inhibitors
INVENTOR(S): Hanson, Sverker; Nordvall, Gunnar; Tiden, Anna-Karin
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003089430 | A1 | 20031030 | WO 2003-SE617 | 20030415 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2480452 | A1 | 20031030 | CA 2003-2480452 | 20030415 |
| AU 2003224548 | A1 | 20031103 | AU 2003-224548 | 20030415 |
| EP 1499613 | A1 | 20050126 | EP 2003-721211 | 20030415 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003009012 | A | 20050201 | BR 2003-9012 | 20030415 |
| CN 1646531 | A | 20050727 | CN 2003-808355 | 20030415 |
| JP 2005526836 | T | 20050908 | JP 2003-586151 | 20030415 |
| NZ 535406 | A | 20060831 | NZ 2003-535406 | 20030415 |
| ZA 2004007815 | A | 20051004 | ZA 2004-7815 | 20040928 |
| US 2005234036 | A1 | 20051020 | US 2004-511537 | 20041015 |
| NO 2004004998 | A | 20050118 | NO 2004-4998 | 20041117 |
| PRIORITY APPLN. INFO.: | | | SE 2002-1193 | A 20020419 |
| | | | SE 2002-2239 | A 20020717 |
| | | | WO 2003-SE617 | W 20030415 |
| OTHER SOURCE(S): MARPAT 139:350580 | | | | |
| ED Entered STN: 31 Oct 2003 | | | | |
| GI | | | | |



I



II

AB Xanthinethiones I and II [one of X and Y = S, the other = O, S; R1, R3, R4 = H, alkyl; R2 = H, (un)substituted alkyl] were prepared for use as myeloperoxidase (MPO) inhibitors in the treatment of neuroinflammatory disorders. Thus, Me2CHCH2NHCSNH2 was cyclized with NCCH2CO2Et to give 6-amino-1-isobutyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one which was nitrosated, reduced to the 5,6-diamine, and cyclized with HCO2H to give II [R1, R3, R4 = H, R2 = CH2CHMe2, X = S, Y = O]. This compound had IC50 for inhibition of MPO of 0.87 μ M.

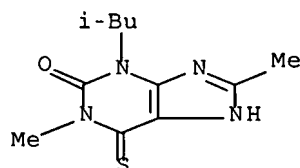
IT 618913-13-6P 618913-15-8P .

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

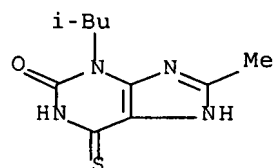
RN 618913-13-6 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1,8-dimethyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



RN 618913-15-8 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-8-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

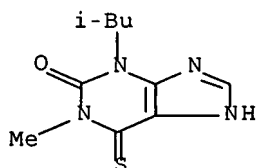
L23 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:413184 CAPLUS Full-text

DOCUMENT NUMBER: 135:251414

TITLE: Structural predictions of adenosine 2B antagonist affinity using molecular field analysis

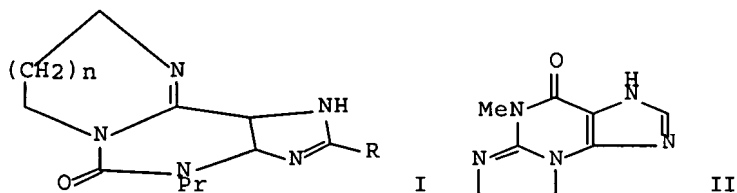
AUTHOR(S): Song, Yuqing; Coupar, Ian M.; Iskander, Magdy N.
 CORPORATE SOURCE: Department of Medicinal Chemistry, Victorian College of Pharmacy, Monash University, Parkville, 3052, Australia
 SOURCE: Quantitative Structure-Activity Relationships (2001), 20(1), 23-30
 CODEN: QSARDI; ISSN: 0931-8771
 PUBLISHER: Wiley-VCH Verlag GmbH
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 08 Jun 2001
 AB 3D structural evaluation of the adenosine 2B (A2B) antagonist binding site is the major aim for developing specific selective antagonists. In an attempt to deduce structural properties of the antagonist site, a pharmacophore model was developed using 85 known A2B antagonists. The mol. mechanics optimization methods were used to deduce the likely binding conformations of the antagonists at the binding site. Super-imposition of the antagonists was carried out using fit-atoms. This alignment was used to develop CoMFA models of the A2B antagonist binding site. The models possessed promising predictive ability as indicated by the high cross-validated correlation ($q^2 = 0.752$, $r^2 = 0.982$) and the prediction on the external test set. The analyses showed that steric and electrostatic interactions contributed to A2B antagonist biol. activity equally. The hydrogen-bond donor nature of the 7-position of xanthine (1 .apprx. 68) and 3-position of alloxazine (83) was essential for the biol. activity. In addition, the presence of more neg. charges on the 1-N position of xanthine and 10-N position of alloxazine increases biol. activity. The bulky aromatic substitutions on the 8-position of xanthine compds. improve activity, while an alkyl substitution on the 1-position of alloxazine might enhance activity. The model generated from this investigation produced important structural requirements, which will be used to optimize the structural complementarity of the antagonists at the A2B binding site.
 IT 42458-91-3, 1-Methyl-3-isobutyl-6-thioxanthine
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (structural predictions of adenosine 2B antagonist affinity using mol. field anal.)
 RN 42458-91-3 CAPLUS
 CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo-(9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1994:77080 CAPLUS Full-text
 DOCUMENT NUMBER: 120:77080
 TITLE: Convenient synthesis of tricyclic purine derivatives
 AUTHOR(S): Shimada, Junichi; Kuroda, Takeshi; Suzuki, Fumio

CORPORATE SOURCE: Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd.,
Shizuoka, 411, Japan
SOURCE: Journal of Heterocyclic Chemistry (1993), 30(1), 241-6
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:77080
ED Entered STN: 19 Feb 1994
GI

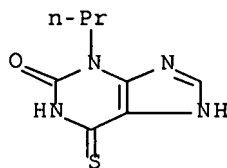


AB A convenient synthesis of the title compds. I (R = H, cyclopentyl; n = 0-2) and II is described. The syntheses of I and II were accomplished by treatment of 6-methylthio-7H-purin-2(3H)-ones or 2-benzylthio-1-methyl-9-triphenylmethyl-9H-purin-6(1H)-one (III) with the appropriate amino alc. followed by dehydrative cyclization using SOCl₂. III was efficiently prepared by benzylation of 6-hydroxy-2-mercaptapurine followed by tritylation and N-methylation.

IT 105396-65-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation of)

RN 105396-65-4 CAPLUS

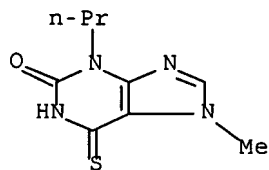
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



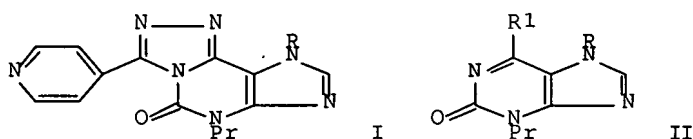
IT 152036-07-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 152036-07-2 CAPLUS

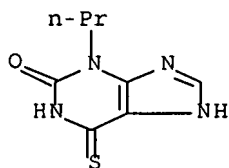
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-7-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1992:469819 CAPLUS Full-text
 DOCUMENT NUMBER: 117:69819
 TITLE: Facile synthesis of 9H-s-triazolo[3,4-i]purin-5(6H)-ones
 AUTHOR(S): Shimada, Junichi; Suzuki, Fumio
 CORPORATE SOURCE: Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411, Japan
 SOURCE: Tetrahedron Letters (1992), 33(22), 3151-4
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 117:69819
 ED Entered STN: 23 Aug 1992
 GI



AB New tricyclic heterocycles, 9H-s-triazolo[3,4-i]purin-5(6H)-ones I (R = Me, H), were prepared from 6-methylthio-7H-purin-2(3H)-ones II (R = Me, PhCH₂OCH₂; R₁ = MeS) via cyclization of II (R₁ = isonicotinoylhydrazino).
 IT 105396-65-4, 3-Propyl-6-thioxanthine
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (methylation or benzylation of)
 RN 105396-65-4 CAPLUS
 CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:536115 CAPLUS Full-text
DOCUMENT NUMBER: 115:136115
TITLE: Preparation of condensed purine derivatives as drugs
INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Kuroda, Takeshi;
Kubo, Kazuhiro; Karasawa, Akira; Ohno, Tetsuji;
Ohmori, Kenji
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| EP 423805 | A2 | 19910424 | EP 1990-120056 | 19901019 |
| EP 423805 | A3 | 19920102 | | |
| EP 423805 | B1 | 20000823 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| CA 2028235 | A1 | 19910421 | CA 1990-2028235 | 19901019 |
| CA 2028235 | C | 19970121 | | |
| JP 03204880 | A | 19910906 | JP 1990-281578 | 19901019 |
| US 5270316 | A | 19931214 | US 1990-599758 | 19901019 |
| AT 195739 | T | 20000915 | AT 1990-120056 | 19901019 |
| ES 2152207 | T3 | 20010201 | ES 1990-120056 | 19901019 |
| | | | JP 1989-273403 | A 19891020 |

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 115:136115

ED Entered STN: 05 Oct 1991

GI For diagram(s), see printed CA Issue.

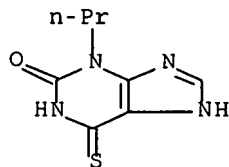
AB Title compds. I (A = Q, Q1, Q2; R1 = H, alkyl, alicyclic alkyl, noradamantan-3-yl, dicyclopropylmethyl, styryl; R2 = H, alkyl, alicyclic alkyl; R3 = H, alkyl, PhCH2; X1, X2 = H, alkyl, aralkyl, Ph; n = 0, 1) or a salt thereof, useful as diuretics, renal protecting agents, bronchodilators or hypotensives, are prepared Thus, H2NCH2CH2OH was added to 3,7-dihydro-7-methyl-6-(methylthio)-3-propyl-2H-purin-2-one (preparation given) and treated at 160° for 1 h to give the hydroxyethylamino derivative which was refluxed with POCl3 and after workup to give the imidazaopurinone II. II showed biol. activity as the above agents. Pharmaceutical formulations are given.

IT 105396-65-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation of)

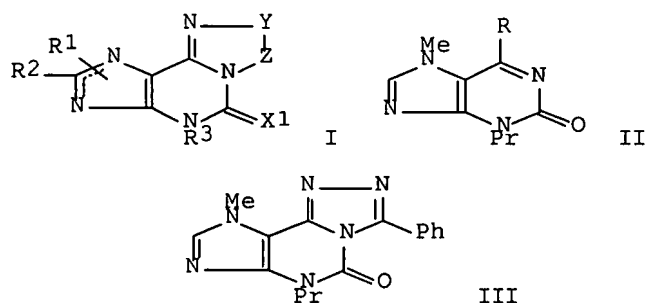
RN 105396-65-4 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



DOCUMENT NUMBER: 115:91963
 TITLE: Preparation and formulation of s-triazolo[3,4-i]purine derivatives as bronchodilators, diuretics, renal protectants, and anti-amnestic agents
 INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Ohmori, Kenji; Manabe, Haruhiko; Kubo, Kazuhiro; Karasawa, Akira; Ohno, Tetsuji; Shiozaki, Shizuo; Ishii, Akio; Shuto, Katsuichi
 PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
 SOURCE: Eur. Pat. Appl., 52 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|------------------|-----------------|-------------|
| EP 417790 | A2 | 19910320 | EP 1990-117662 | 19900913 |
| EP 417790 | A3 | 19920318 | | |
| EP 417790 | B1 | 19961204 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| JP 03204879 | A | 19910906 | JP 1990-243248 | 19900913 |
| JP 2980658 | B2 | 19991122 | | |
| AT 145908 | T | 19961215 | AT 1990-117662 | 19900913 |
| ES 2097124 | T3 | 19970401 | ES 1990-117662 | 19900913 |
| CA 2025413 | A1 | 19910315 | CA 1990-2025413 | 19900914 |
| CA 2025413 | C | 19971104 | | |
| US 5173492 | A | 19921222 | US 1991-752180 | 19910823 |
| PRIORITY APPLN. INFO.: | | | JP 1989-239117 | A 19890914 |
| | | | JP 1989-261761 | A 19891006 |
| | | | US 1990-581562 | B1 19900912 |
| OTHER SOURCE(S): | | MARPAT 115:91963 | | |
| ED Entered STN: | | 06 Sep 1991 | | |
| GI | | | | |



AB The title compds. [I; R1, R2 = H, alkyl, cycloalkyl, aralkyl, (substituted) aryl; R3 = alkyl, cycloalkyl, aralkyl, (substituted) aryl; X1 = O, S; YZ = N:CR4 or NR4C(:X2) wherein R4 = H, alkyl, (substituted) (hetero)aryl, X2 = O, S, NH] are prepared PhCONHNH2 was added to a suspension of II (R = MeS) (preparation given) in MePh, the mixture was refluxed to give 60% hydrazine

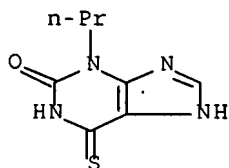
derivative II (R = PhCONHNH), which (2.64 g) was refluxed with 308 mg p-MeC₆H₄SO₃H in MePh to give 67% title compound III. III showed IC₅₀ of 4.1 μ M in passive Schultz-Dale reaction (bronchodilatory effects) and diuretic activity at 25 mg/kg orally in rats. Also prepared and tested were 50 addnl. I. Tablet, syrup, powder, and capsule formulations were also given.

IT 105396-65-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of triazolopurine drugs)

RN 105396-65-4 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)

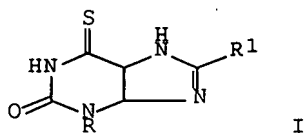


L23 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1986:626214 CAPLUS Full-text
 DOCUMENT NUMBER: 105:226214
 TITLE: 6-Thioxanthine derivatives
 INVENTOR(S): Hofer, Peter
 PATENT ASSIGNEE(S): Euro-Celtique S. A., Luxembourg
 SOURCE: Eur. Pat. Appl., 7 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| EP 191313 | A1 | 19860820 | EP 1986-100544 | 19860117 |
| EP 191313 | B1 | 19921028 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| US 4710503 | A | 19871201 | US 1985-699254 | 19850207 |
| IN 161914 | A1 | 19880227 | IN 1985-CA906 | 19851218 |
| ZA 8509805 | A | 19860827 | ZA 1985-9805 | 19851223 |
| IL 77430 | A | 19881031 | IL 1985-77430 | 19851224 |
| AU 8651840 | A | 19860814 | AU 1986-51840 | 19860103 |
| AU 570142 | B2 | 19880303 | | |
| AT 81858 | T | 19921115 | AT 1986-100544 | 19860117 |
| FI 8600285 | A | 19860808 | FI 1986-285 | 19860121 |
| FI 84180 | B | 19910715 | | |
| FI 84180 | C | 19911025 | | |
| DK 8600332 | A | 19860808 | DK 1986-332 | 19860122 |
| DK 161964 | B | 19910902 | | |
| DK 161964 | C | 19920210 | | |
| CN 86101050 | A | 19861112 | CN 1986-101050 | 19860205 |
| CN 1013676 | B | 19910828 | | |
| NO 8600424 | A | 19860808 | NO 1986-424 | 19860206 |
| NO 163569 | B | 19900312 | | |

| | | | | |
|------------------------|----|----------|----------------|-------------|
| NO 163569 | C | 19900620 | | |
| CA 1275288 | C | 19901016 | CA 1986-501288 | 19860206 |
| JP 61183287 | A | 19860815 | JP 1986-24248 | 19860207 |
| JP 07080882 | B | 19950830 | | |
| US 4820709 | A | 19890411 | US 1987-75937 | 19870722 |
| US 4925847 | A | 19900515 | US 1987-78545 | 19870728 |
| US 5010081 | A | 19910423 | US 1989-415970 | 19891002 |
| JP 08099882 | A | 19960416 | JP 1995-6756 | 19950119 |
| JP 2888273 | B2 | 19990510 | | |
| PRIORITY APPLN. INFO.: | | | US 1985-699254 | A 19850207 |
| | | | EP 1986-100544 | A 19860117 |
| | | | GB 1986-18931 | A 19860802 |
| | | | US 1987-78545 | A1 19870728 |
| | | | US 1989-322364 | B2 19890313 |

OTHER SOURCE(S): CASREACT 105:226214
ED Entered STN: 26 Dec 1986
GI

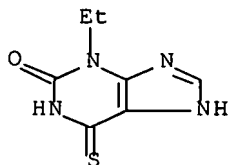


AB The title compds. I (R = Et, Pr, Bu; R1 = H, Me, Et) useful as bronchodilators (no data) were prepared. Thus, 3-ethylxanthine in pyridine was treated with P2S5, H2O, NaOH, and acidified with 5N HCl to give I (R = Et; R1 = H).

IT 105396-64-3P 105396-65-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as bronchodilator)

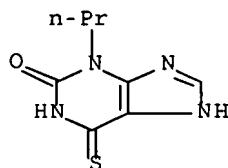
RN 105396-64-3 CAPLUS

CN 2H-Purin-2-one, 3-ethyl-1,3,6,7-tetrahydro-6-thioxo- (9CI) (CA INDEX NAME)

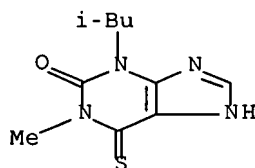


RN 105396-65-4 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)

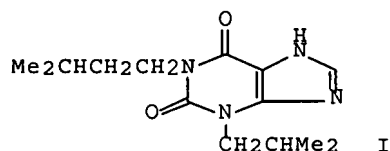


L23 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1981:435269 CAPLUS Full-text
 DOCUMENT NUMBER: 95:35269
 TITLE: Adenosine antagonism by purines, pteridines, and benzopteridines in human fibroblasts
 AUTHOR(S): Bruns, Robert F.
 CORPORATE SOURCE: Dep. Neurosci., Univ. California, La Jolla, CA, 92093, USA
 SOURCE: Biochemical Pharmacology (1981), 30(4), 325-33
 CODEN: BCPA6; ISSN: 0006-2952
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 12 May 1984
 AB Testing of >100 purine bases and structurally related heterocycles as adenosine (I) [58-61-7] antagonists in VA13 fibroblasts (determined by cAMP increase) yielded 3 families of I antagonists: xanthines, benzo[g]pteridines, and 9-substituted adenines. For the xanthines, the optimal group at the 1-position was Bu (5-fold improvement vs. Me), at the 7-position was 2-chloroethyl (5-fold improvement vs. H), and at the 8-position was p-bromophenyl (100-fold improvement vs. H). The receptors apparently had butyl- and phenyl-sized pockets at the 1- and 8-positions, resp., since compds. with larger groups had greatly reduced activity.
 IT 42458-91-3
 RL: BIOL (Biological study)
 (adenosine receptor of fibroblast antagonism by)
 RN 42458-91-3 CAPLUS
 CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo-(9CI) (CA INDEX NAME)



L23 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1980:51769 CAPLUS Full-text
 DOCUMENT NUMBER: 92:51769
 TITLE: Effects of phosphodiesterase inhibitors on cyclic nucleotide levels and relaxation of pig coronary arteries
 AUTHOR(S): Kramer, G. L.; Wells, J. N.
 CORPORATE SOURCE: Sch. Med., Vanderbilt Univ., Nashville, TN, 37232, USA

SOURCE: Molecular Pharmacology (1979), 16(3), 813-22
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI



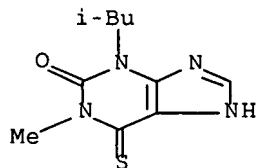
AB A series of xanthine derivs. and papaverine were studied to determine their abilities to alter tissue levels of cyclic AMP [60-92-4] and cyclic GMP [7665-99-8], inhibit cyclic nucleotide phosphodiesterase [50812-31-2] activities, and cause relaxation of pig coronary arteries. The agents exhibited a wide range of potencies to inhibit phosphodiesterase activities in the coronary artery supernatant fraction. In addition, some of these agents were up to 10 times more potent as inhibitors of cyclic GMP hydrolysis than of cyclic AMP hydrolysis, whereas others were 2-4 times more potent as inhibitors of cyclic AMP than of cyclic GMP hydrolysis. The rank order of potencies of these agents to cause relaxation of coronary artery strips was similar to the rank order of potencies to inhibit cyclic nucleotide phosphodiesterase activities. There were, however, some notable exceptions to the correlation between inhibition of cyclic nucleotide phosphodiesterase activities and relaxation. 1-Isoamyl-3-isobutylxanthine (I) [63908-26-9] was a more potent relaxing agent than might be expected from its relatively low potency to inhibit cyclic nucleotide hydrolysis in tissue exts. On the other hand, 1-methyl-3-isobutyl-7-(3-chlorobenzyl)-xanthine [58481-28-0] was 1 of the more potent inhibitors of cyclic nucleotide hydrolysis but was not as potent in causing relaxation as might have been expected. Exposure of the coronary artery strips to inhibitors caused increase in tissue levels of cyclic AMP and cyclic GMP and there was a statistically significant multiple linear regression of cyclic AMP and cyclic GMP levels on percent relaxation after 5 min of exposure to the agents. Cyclic AMP and cyclic GMP levels made approx. equal contributions to the regression of changes in percent relaxation, as determined by anal. of variance methods. While I did not fit the correlation between phosphodiesterase inhibition and potency to relax the arterial strips as well as the other agents, this agent caused unexpectedly large increases in cyclic AMP levels. Some agents caused relaxation accompanied by significant elevation of cyclic GMP levels and no significant change in cyclic AMP levels while other agents caused relaxation accompanied by significant increases in cyclic AMP but not cyclic GMP. These data offer some support for a hypothesis that both cyclic AMP and cyclic GMP are involved in the relaxation processes of pig coronary arteries.

IT 42458-91-3

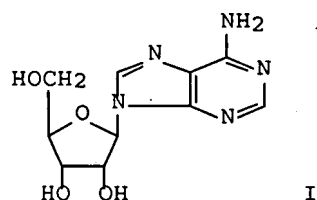
RL: BIOL (Biological study)
(cyclic nucleotide of artery and artery contraction response to)

RN 42458-91-3 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo-
(9CI) (CA INDEX NAME)



L23 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1977:133356 CAPLUS Full-text
 DOCUMENT NUMBER: 86:133356
 TITLE: Effects of adenosine and related compounds on
 adenylyl cyclase and cyclic AMP levels in smooth
 muscle
 AUTHOR(S): McKenzie, Sheila G.; Frew, Robert; Bar, Hans P.
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Alberta, Edmonton, AB, Can.
 SOURCE: European Journal of Pharmacology (1977), 41(2),
 193-203
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 12 May 1984
 GI

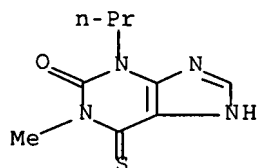


AB The hypotheses were tested that the relaxant effect of adenosine (I) [58-61-7] and related compds. in the longitudinal muscle of the rabbit small intestine involves interaction with adenylyl cyclase [9012-42-4] and/or the elevation of tissue cyclic AMP [60-92-4] levels. Adenylyl cyclase was prepared by gentle homogenization of an isolated smooth muscle cell fraction obtained after collagenase digestion of longitudinal muscle strips. A number of analogs and derivs. of I possessing a primary or secondary 6-amino group inhibited the enzyme similarly to I; however, there was no correlation between compds. known to relax the intact tissue and the existence, or the degree of, cyclase inhibition. Isolated muscle strips were exposed to adrenaline bitartrate [51-42-3], DL-isoprenaline-HCl [949-36-0], I, or ATP [56-65-5], at doses causing 30-60% relaxation, for 60 s prior to sampling and anal. of cAMP content. While small increments in cAMP levels were found after administering adrenaline or isoprenaline, no change was found with I in the absence or presence of aminophylline [317-34-0] or 1-methyl-3-isobutylxanthine [28822-58-4]. Neither adenylyl cyclase inhibition nor changes in cAMP levels appear to be part of the mechanism of the smooth muscle relaxant action of I or ATP.

IT 42458-88-8 42458-91-3
 RL: BIOL (Biological study)
 (adenylyl cyclase of intestine smooth muscle response to)

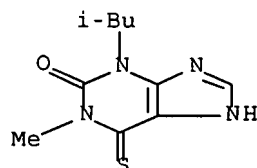
RN 42458-88-8 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



RN 42458-91-3 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1977:133355 CAPLUS Full-text

DOCUMENT NUMBER: 86:133355

TITLE: Characteristics of the relaxant response of adenosine and its analogs in intestinal smooth muscle

AUTHOR(S): McKenzie, Sheila G.; Frew, Robert; Bar, Hans P.

CORPORATE SOURCE: Dep. Pharmacol., Univ. Alberta, Edmonton, AB, Can.

SOURCE: European Journal of Pharmacology (1977), 41(2), 183-92

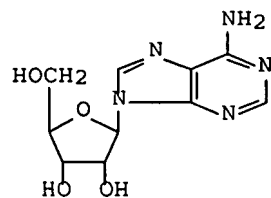
CODEN: EJPHAZ; ISSN: 0014-2999

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 May 1984

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I

AB Several characteristics of the relaxant response of the isolated longitudinal muscle of the rabbit small intestine in response to the administration of adenosine (I) [58-61-7] and related compds. are studied. Following administration of I or ATP [56-65-5] the preparation responded with a rapid initial suspension of spontaneous contractile activity followed by a secondary sustained phase of inhibition of lower magnitude. Cumulative application of relaxant doses of I or ATP caused a lesser total response than that obtained by single application of the cumulative dose. Neither procaine, lidocaine or guanethidine antagonized the responses to I or ATP and the responsiveness of muscles obtained from reserpinized animals appeared unchanged. A number of I derivs. and analogs was tested for the ability to relax the muscle. Generally, compds. containing a primary or secondary 6-amino group acted as agonists with the exception of 8-bromoadenosine [2946-39-6]. Inactive nucleosides did not modify the responsiveness of the muscle to I. Responses to I and ATP were not appreciably modified by papaverine, imidazole, dipyridamole, 6-(p-nitrobenzylthio)-purine riboside. Antagonism was observed, however, with phentolamine [50-60-2] and aminophylline [317-34-0]. Aminophylline at 100 μ M inhibited responses to I over a wide dose range; this antagonism was surmountable by high doses of I. 1-Methyl-3-isobutylxanthine [28822-58-4] did not antagonize I responses. A number of 1,3-alkyl-6-thioxanthines did not modify the I response at doses that did not show any direct action. The results support the concept of an extracellular receptor site of I and its analogs and the absence of an indirect mechanism of action via nerve stimulation.

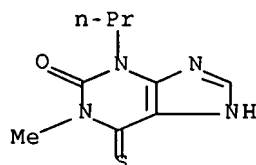
IT 42458-88-8 42458-91-3

RL: BIOL (Biological study)

(intestine smooth muscle relaxation by adenosine and its analogs response to)

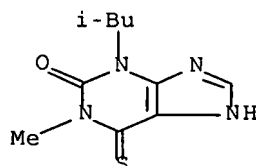
RN 42458-88-8 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



RN 42458-91-3 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1976:130133 CAPLUS Full-text
DOCUMENT NUMBER: 84:130133
TITLE: Inhibition of separated forms of phosphodiesterases from pig coronary arteries by uracils and by 7-substituted derivatives of 1-methyl-3-isobutylxanthine
AUTHOR(S): Garst, J. E.; Kramer, G. L.; Wu, Y. J.; Wells, J. N.
CORPORATE SOURCE: Sch. Med., Vanderbilt Univ., Nashville, TN, USA
SOURCE: Journal of Medicinal Chemistry (1976), 19(4), 499-503
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
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Rehs 8-14

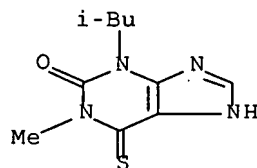
AB A series of 15 title xanthine derivs. (I; R = alkyl, aralkyl, alicyclicalkyl, propargyl, 4-picoly), prepared by alkylation of 1-methyl-3-isobutylxanthine (I, R = H) (MIX) [28822-58-4] were tested for specificity of inhibition of chromatog.-separated cyclic nucleotide phosphodiesterase [50812-31-2] activity fractions I and II. I were generally much less potent than MIX as inhibitors of activity fraction II, but some retained the potency of MIX as inhibitors of activity fraction I. 1-Methyl-3-isobutyl-7-benzylxanthine (I, R = PhCH₂) [58481-23-5] was 20-30 times more potent as an inhibitor of activity fraction I than of II, while retaining the potency of MIX against activity fraction I. A series of 1,3-dialkyluracils had low potency as phosphodiesterase inhibitors. Structure-activity relations were discussed.

IT 42458-91-3

RL: BIOL (Biological study)
(cyclic nucleotide phosphodiesterases inhibition by)

RN 42458-91-3 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1973:427084 CAPLUS Full-text

DOCUMENT NUMBER: 79:27084

TITLE: Structure-activity relations. III. Bronchodilator

activity of substituted 6-thioxanthines

AUTHOR(S): Bowden, Keith; Wooldridge, Kenneth R. H.
 CORPORATE SOURCE: Dep. Chem., Univ. Essex, Colchester/Essex, UK
 SOURCE: Biochemical Pharmacology (1973), 22(9), 1015-21
 CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal
 LANGUAGE: English

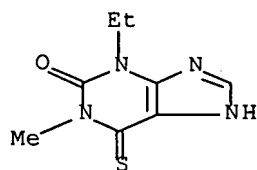
ED Entered STN: 12 May 1984

AB A correlation of the bronchodilator activity of a series of substituted 6-thioxanthines (I) was made with partition parameters and (or) the steric effect of the 1- and 3-substituents. An increase in activity was observed on introduction of bulky substituents at R3 and particularly at R1. The 3-substituted series were also correlated by a Hansch relation involving partition factors alone. Thus, 1,3-dibutyl-6-thioxanthine [40915-18-2] was far more active than 1,3-dimethyl-6-thioxanthine [2398-70-1].

IT 42458-87-7 42458-88-8 42458-91-3
 42458-96-8
 RL: BIOL (Biological study)
 (bronchodilator)

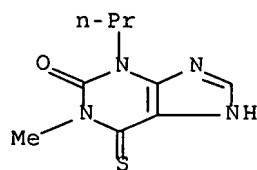
RN 42458-87-7 CAPLUS

CN 2H-Purin-2-one, 3-ethyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA INDEX NAME)



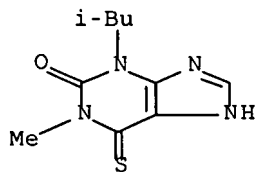
RN 42458-88-8 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



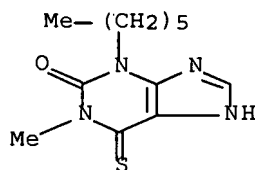
RN 42458-91-3 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



RN 42458-96-8 CAPLUS

CN 2H-Purin-2-one, 3-hexyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:429662 CAPLUS Full-text

DOCUMENT NUMBER: 57:29662

ORIGINAL REFERENCE NO.: 57:5924h-i,5925a-i,5926a-b

TITLE: The synthesis of some 6-thioxanthines

AUTHOR(S): Wooldridge, K. R. H.; Slack, R.

CORPORATE SOURCE: May Baker Ltd., Dagenham, UK

SOURCE: Journal of the Chemical Society (1962) 1863-28

CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 57:29662

ED Entered STN: 22 Apr 2001

AB A series of 1,3- and 3,7-disubstituted 6-thioxanthines, of interest as broncho and coronary dilators, has been prepared by the selective thionation of the corresponding xanthines with P2S5 in C5H5N. 1,3,7-Trialkyl-6- thioxanthines could not be prepared in this way but were readily obtained from 1,3-dialkyl-6-thioxanthines. Theophylline (50 g.), 100 g. P2S3, and 1. dry C5H5N refluxed 8 hrs. with stirring, cooled, diluted with stirring during 1 hr. with 2 l. H2O, concentrated to about 1/3 volume, cooled, and filtered, and the residue dissolved in 2N NaOH, filtered, and reprecipitated with dilute HCl yielded 51 g. 1,3-dimethyl-6-thioxanthine (I), pale yellow needles, m. 323-5° (decomposition) (EtOH or H2O). 6-Thiotheobromine (75 g.) with 150 g. P2S5 gave similarly 72 g. 3,7-dimethyl-6-thioxanthine (II), m. 300-1°. (MeNH)2CS (79 g.) added in portions with stirring during 0.5 hr. to 65 g. NCCH2CO2H in 156 g. Ac2O and 200 cc. AcOH at 65°, kept 2 hrs. at 65% evaporated at 69-5° in vacuo, and the gummy residue stirred at 50° with 200 cc. H2O and adjusted to pH 10 with 50% aqueous NaOH gave 65 g. 6-amino-1,3-dimethyl 2-thiouracil (III), prisms, m. 286-8° (EtOH). The crude III suspended in 6000 cc. H2O containing 25.5 g. NaNO2 at 80-90 °, 50 cc. AcOH added during 15 min., and the mixture stirred 15 min. at 80-90° and cooled yielded crude 5-NO derivative (IV) of III, blue-green amorphous solid, m. 215-16° (decomposition). The IV added in 5-g. portions to 2.5 l. H2O at 70-80° together with sufficient Na2S2O4 to discharge the color of the IV, cooled, and filtered, the residual 5-NH2 derivative of

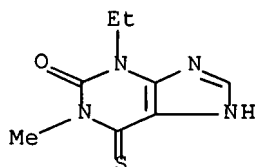
III, m. 230-4°, added immediately to 500 cc. 2N H₂SO₄, the resulting sulfate (57 g.) boiled 0.5 hr. with 500 cc. HCONH₂, diluted with 250 cc. H₂O, and cooled, and the yellow solid dissolved in 300 cc. hot 17% NH₄OH, filtered, and acidified to pH 4 with AcOH yielded 47 g. 1,3dimethyl-2-thioxanthine, m. 344-8°. Me₂SO₄ (25.2 g.) added dropwise in 15 min. with stirring at 40° to 35 g. I and 100 cc. 2N NaOH, kept 0.5 hr. at 40°, cooled, and filtered gave 15 g. 1,3,7-trimethyl-6-thioxanthine (V), pale yellow prisms, m. 246-7°. II (17.5 g.) and 42.5 g. Me₂SO₄ gave 1 g. V, m. 247-9°. II (10g.) in 125 cc. 0.5N NaOH stirred 2 hrs. at room temperature with 10.7 g. MeI yielded 6.7 g. 1,2,3,4tetrahydro-3,7-dimethyl- 1-methylthiopurine, needles, m. 300-3° (H₂O). The appropriate urea was converted by the method of Traube [Ber. 33, 3035(1900)] or of Speer and Raymond (CA 48, 1346h) or of Montgomery (CA 50, 13932b) to the corresponding 1,3-dialkylxanthines. (1- and 3-alkyl group and m.p. given): Me, MeO(CH₂)₃, 166-8°; Me, furfuryl, 255-8°; Et, iso-Bu, 195-7°; Pr, iso-Bu, 189-92°; Bu, Me, 207-10°. Similarly were prepared 3-isobutylxanthine (VI), m. 299-301°, and the 7-Me derivative of VII, m. 239-41°. P₂S₅ (600 g.) and 482 g. 3-isobutyl-1-methylxanthine in 4.2 l. dry C₅H₅N, refluxed 9 hrs. with stirring, cooled to about 40°, diluted carefully with H₂O, concentrated to about 2.5 l., diluted with 3.5 l. H₂O, and filtered, and the residue dissolved in 2.5 l. warm N NaOH, filtered, and acidified with concentrated HCl to pH 4 pp.d. 426 g. 3-isobutyl-1-methyl-6-thioxanthine (VII), yellow prisms, m. 170-2° (EtOH). Similarly were prepared the following 1,3-disubstituted-6-thioxanthines (1- and 3-substituent, m.p., and % yield given): Me, Me (VIII), 3235°, 94; Me, Et, 235-7°, 79; Me, Pr, 164-7°, 63; Me, Bu, 156-8°, 73; Me, Am, 169-70°, 50; Me, C₆H₁₃, 167-74°, 78; Me, iso-Am, 156-60°, 50; Me, MeO(CH₂)₃, 150-2°, 50; Me, CH₂:CHCH₂, 152-6°, 81; Me, CH:CMech₂, 195-8°, 47; Me, PhCH₂, 213-15°, 84; Me, Ph(CH₂)₂, 198-9°, 63; Me, furfuryl, 184-6°, 15; Et, Me, 235-9°, 76; Et, Et, 2568°, 72; Et, Bu, 175-8°, 74; Et, iso-Bu, 180-3°, 39; Et, CH₂:CHCH₂, 210-12°, 49; Pr, Pr, 212-15°, 89; Bu, Me, 295-8°, 84; Bu, Bu, 183-6°, 72. Similarly were prepared the following 8-substituted VIII (substituent, m.p., and % yield given): Me, 294-5°, 75; Et, 218-19°, 76; SH, 240° (decomposition), 83. I (42 g.) and 8.6 g. NaOH in 150 cc. H₂O stirred 0.5 hr. at room temperature, cooled, and filtered, and the dried Na salt (44 g.) of I dissolved in 200 cc. HCONMe₂, treated with stirring during 15 min. at room temperature with 18.6 g. AcCH₂Cl, stirred 0.5 hr., diluted with 300 cc. iced H₂O, and filtered gave 21.3 g. 7-AcCH₂ derivative (IX) of I, yellow needles, m. 208-10°. IX (21 g.), 269 g. paraformaldehyde, 11.9 g. piperidine-HCl, 1.6 cc. Et₂O.BF₃, and 200 cc. dry dioxane stirred 7 hrs. at 100° and filtered gave 23.0 g. 1,3-dimethyl-7(2-oxo-4-piperidinobutyl)-6-thioxanthine-HCl, yellow-brown prisms, m. 197-200°. In the same manner as VII were prepared the following 1,3,7-trisubstituted-6-thioxanthines (1-, 3-, and 7-substituents and m.p. given): Me, Me, Et, 22830°; Me, Me, Et₂N(CH₂)₂, 52-4°; Me, iso-Bu, Et₂N(CH₂)₂ [isolated as the (-)-di(p-toluoyl) D-tartrate], 120° (decomposition); Me, iso-Bu, AcCH₂, 170-4°; Bu, Me, Me, 118-19°. in the same manner were prepared the following 3,7-dialkyl-6thioxanthines (3- and 7-substituents and m.p. given): Me, Me, 300-1°; Bu, Me, 200-3°; iso-Bu, Me, 228-30°. Also prepared was 3-methyl-6-thioxanthine, m. 269-74°. Choline chloride (3.4 g.) in 900 cc. hot iso-PrOH treated with stirring with 150 g. 85% KOH in 600 cc. absolute MeOH, cooled to 0°, filtered, treated with 500 g. VII, warmed a few min., and evaporated in vacuo, the residual sirup dissolved in 1 l. hot isoPrOH, treated with C, filtered, diluted with 1 l. dry Et₂O, and cooled, and the precipitated filtered off gave 548 g. choline salt of VII, pale yellow prisms, m. 145-9°; their mother liquor evaporated, and the sirupy residue dissolved in H₂O and acidified to pH 4 with HCl gave 8 g. VII. Similarly were prepared the choline salts of the following 1,3-disubstituted-6-thioxanthines (1- and 3-substituents, m.p. and % yield given): Me, Me (X), 145-7°, 47; Me, Et, 157-9°, 72; Me, Pr, 145-50°, 72; Me, Bu, 133-5°, 88; Me, Am, 150-3°, 93; Me, C₆H₁₃, 55-7°, 94; Me, iso-Bu, 148.5-9.5°, 92; Me, iso-Am, 125-8°, 90; Me, CH₂:CHCH₂, 172-5°, 73; Me, CH₂:CMech₂,

145-51°, 80; Me, PhCH₂, 166-71°, 80; Me, Ph(CH₂)₂, 173-5°, 80; Et, Me, 157-8°, 70; Et, Et, 142-7°, 92; Et, Bu, 115-18°, 79; Pr, Pr, 114-18°, 57; Bu, Me, 105-9°, 62. Also prepared were 8-Me derivative of X, 175-6°, 65, and the 8-SH derivative of X, 209 11°, 70. The ultraviolet absorption maximum of a number of thioxanthines are tabulated.

IT 42458-87-7P, Xanthine, 3-ethyl-1-methyl-6-thio-
 42458-88-8P, Xanthine, 1-methyl-3-propyl-6-thio-
 42458-91-3P, Xanthine, 3-isobutyl-1-methyl-6-thio-
 42458-96-8P, Xanthine, 3-hexyl-1-methyl-6-thio-
 93263-24-2P, Xanthine, 3-isobutyl-6-thio- 94733-95-6P,
 Heteroxanthine, 3-isobutyl-6-thio- 96536-20-8P, Choline, compound
 with 3-ethyl-1-methyl-6-thioxanthine 97212-72-1P, Choline,
 compound with 1-methyl-3-propyl-6-thioxanthine 97406-00-3P,
 Choline, compound with 3-isobutyl-1-methyl-6-thioxanthine
 98174-21-1P, Choline, compound with 3-hexyl-1-methyl-6-thioxanthine
 RL: PREP (Preparation)
 (preparation of)

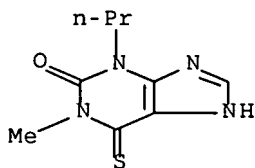
RN 42458-87-7 CAPLUS

CN 2H-Purin-2-one, 3-ethyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA
 INDEX NAME)



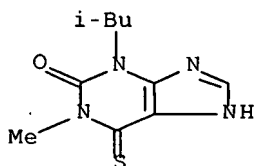
RN 42458-88-8 CAPLUS

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-propyl-6-thioxo- (9CI) (CA
 INDEX NAME)

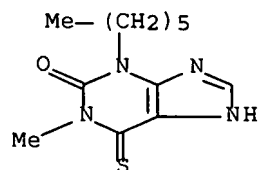


RN 42458-91-3 CAPLUS

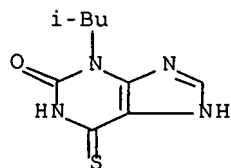
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo-
 (9CI) (CA INDEX NAME)



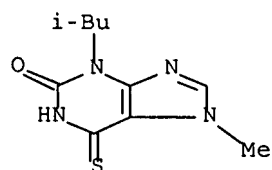
RN 42458-96-8 CAPLUS
CN 2H-Purin-2-one, 3-hexyl-1,3,6,7-tetrahydro-1-methyl-6-thio- (9CI) (CA INDEX NAME)



RN 93263-24-2 CAPLUS
CN Xanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



RN 94733-95-6 CAPLUS
CN Heteroxanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



RN 96536-20-8 CAPLUS
CN Choline, compd. with 3-ethyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

CM 1

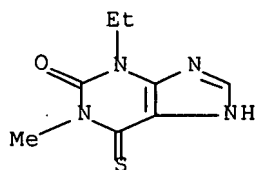
CRN 44519-34-8

CMF C5 H13 N O

Me₃N-CH₂-CH₂-O-

CM 2

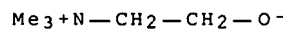
CRN 42458-87-7
CMF C8 H10 N4 O S



RN 97212-72-1 CAPLUS
CN Choline, compd. with 1-methyl-3-propyl-6-thioxanthine (7CI) (CA INDEX NAME)

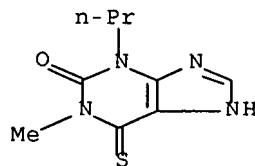
CM 1

CRN 44519-34-8
CMF C5 H13 N O



CM 2

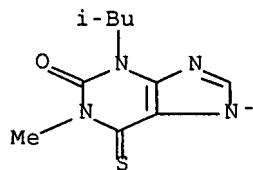
CRN 42458-88-8
CMF C9 H12 N4 O S



RN 97406-00-3 CAPLUS
CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

CM 1

CRN 97405-99-7
CMF C10 H13 N4 O S



CM 2

CRN 62-49-7

CMF C5 H14 N O

$\text{Me}_3\text{N}-\text{CH}_2-\text{CH}_2-\text{OH}$

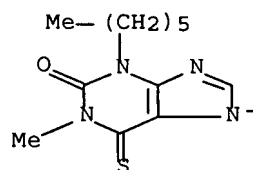
RN 98174-21-1 CAPLUS

CN Choline, compd. with 3-hexyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

CM 1

CRN 98174-20-0

CMF C12 H17 N4 O S



CM 2

CRN 62-49-7

CMF C5 H14 N O

$\text{Me}_3\text{N}-\text{CH}_2-\text{CH}_2-\text{OH}$

L23 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1963:48836 CAPLUS [Full-text](#)

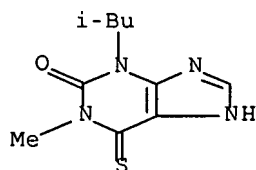
DOCUMENT NUMBER: 58:48836

ORIGINAL REFERENCE NO.: 58:8327a-b

TITLE: Observations concerning the effects of a thioxanthine upon the heart of the intact animal

AUTHOR(S): Maxwell, G. M.; Elliott, R. B.; Kneebone, G. M.

CORPORATE SOURCE: Univ. Adelaide
SOURCE: Australian J. Exp. Biol. Med. Sci. (1962), 40, 335-40
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB An intravenous dose of 1.0 mg. 3-isobutyl-1-methyl-6-thioxanthine/kg. administered to dogs gave statistically significant increases in respiratory rate, respiratory volume, O consumption, CO2 production, and pulse rate. Femoral and pulmonary arterial pressures decreased as did the calculated total peripheral resistance. Coronary blood flow and cardiac metabolic rates for O and CO2 increased. Cardiac efficiency and coronary vascular resistance decreased.
IT 42458-91-3, Xanthine, 3-isobutyl-1-methyl-6-thio-
(heart response to)
RN 42458-91-3 CAPLUS
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo-
(9CI) (CA INDEX NAME)



L23 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:41798 CAPLUS Full-text
DOCUMENT NUMBER: 56:41798
ORIGINAL REFERENCE NO.: 56:7935c-f
TITLE: Structure-activity relations in a series of
6-thioxanthines with bronchodilator and coronary
dilator properties
AUTHOR(S): Armitage, A. K.; Boswood, Janet; Large, B. J.
SOURCE: British Journal of Pharmacology and Chemotherapy
(1961), 17, 196-207
CODEN: BJPCAL; ISSN: 0366-0826
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB The bronchodilator, coronary dilator, central stimulant, and diuretic activities of forty-seven 1,3-and 3,7-disubstituted and 1,3,7-trisubstituted 6-thioxanthines are reported. Bronchodilator activity was determined on the isolated guinea pig tracheal ring preps. and coronary dilator activity on the dog heart-lung preps. Diuretic activity was determined using conscious rats, and stimulant activity using mice. The in vivo bronchodilatory activity was determined by the protection afforded to guinea pigs against bronchoconstrictor aerosol. While choline 6-thiotheophyllinate is twice as active as choline theophyllinate as a broncho- and coronary dilator, several higher members of the theophylline series are more active than the 6-thio analogs. The 6-thiotheophylline is more active than the 6-thiotheobromine and 6-thiocaffeine. The 1,3-disubstituted compds. were more active as broncho- and coronary dilators than the 3,7-substituted compds. Maximum bronchodilator activity was achieved with relatively large alkyl groups in the 1 and 3 positions, and the 3-isobutyl derivative of 1-methyl-6-thiotheophylline was most active. Large groups in the 1-position may reduce oral absorption.

Compds. with unsatd. or substituted alkyl groups in the 3-position are less bronchoactive than compds. containing the corresponding saturated or unsubstituted groups. A 1-methyl group may be essential for coronary dilator activity. All the compds. tested had low diuretic activity. 6-Thiocaffeines, in contrast to caffeine, show no stimulant properties.

IT 96536-20-8, Choline, compound with 3-ethyl-1-methyl-6-thioxanthine
 97212-72-1, Choline, compound with 1-methyl-3-propyl-6-thioxanthine
 97406-00-3, Choline, compound with 3-isobutyl-1-methyl-6-thioxanthine 98174-21-1, Choline, compound with
 3-hexyl-1-methyl-6-thioxanthine
 (blood vessel and bronchial dilation by)

RN 96536-20-8 CAPLUS

CN Choline, compd. with 3-ethyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

CM 1

CRN 44519-34-8

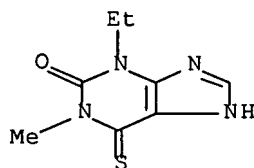
CMF C5 H13 N O

$\text{Me}_3\text{N}-\text{CH}_2-\text{CH}_2-\text{O}^-$

CM 2

CRN 42458-87-7

CMF C8 H10 N4 O S



RN 97212-72-1 CAPLUS

CN Choline, compd. with 1-methyl-3-propyl-6-thioxanthine (7CI) (CA INDEX NAME)

CM 1

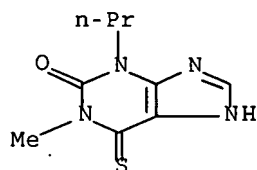
CRN 44519-34-8

CMF C5 H13 N O

$\text{Me}_3\text{N}-\text{CH}_2-\text{CH}_2-\text{O}^-$

CM 2

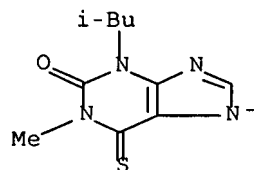
CRN 42458-88-8
CMF C9 H12 N4 O S



RN 97406-00-3 CAPLUS
CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

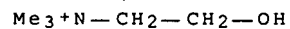
CM 1

CRN 97405-99-7
CMF C10 H13 N4 O S



CM 2

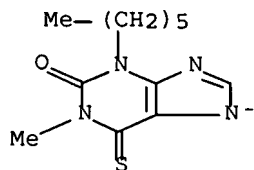
CRN 62-49-7
CMF C5 H14 N O



RN 98174-21-1 CAPLUS
CN Choline, compd. with 3-hexyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

CM 1

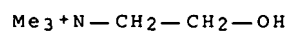
CRN 98174-20-0
CMF C12 H17 N4 O S



CM 2

CRN 62-49-7

CMF C5 H14 N O

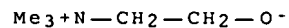


IT 96536-20-8, Xanthine, 3-ethyl-1-methyl-6-thio-, compound with
choline 97212-72-1, Xanthine, 1-methyl-3-propyl-6-thio-, compound
with choline 98174-21-1, Xanthine, 3-hexyl-1-methyl-6-thio-,
compound with choline
(blood-vessel and bronchial dilation by)
RN 96536-20-8 CAPLUS
CN Choline, compd. with 3-ethyl-1-methyl-6-thioxanthine (7CI) (CA INDEX
NAME)

CM 1

CRN 44519-34-8

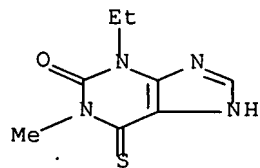
CMF C5 H13 N O



CM 2

CRN 42458-87-7

CMF C8 H10 N4 O S

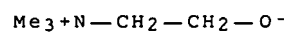


RN 97212-72-1 CAPLUS
CN Choline, compd. with 1-methyl-3-propyl-6-thioxanthine (7CI) (CA INDEX
NAME)

CM 1

CRN 44519-34-8

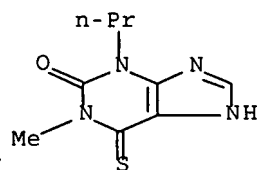
CMF C5 H13 N O



CM 2

CRN 42458-88-8

CMF C9 H12 N4 O S



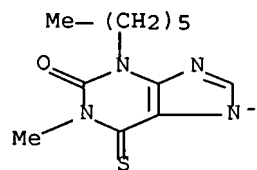
RN 98174-21-1 CAPLUS

CN Choline, compd. with 3-hexyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

CM 1

CRN 98174-20-0

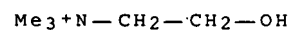
CMF C12 H17 N4 O S



CM 2

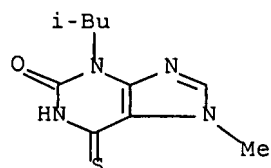
CRN 62-49-7

CMF C5 H14 N O

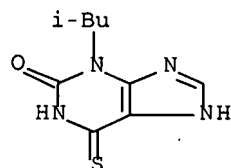


IT 94733-95-6, Heteroxanthine, 3-isobutyl-6-thio-

(sodium derivative, blood vessel and bronchial dilation by)
RN 94733-95-6 CAPLUS
CN Heteroxanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



IT 93263-24-2, Xanthine, 3-isobutyl-6-thio-
(sodium derivative, blood-vessel and bronchial dilation by)
RN 93263-24-2 CAPLUS
CN Xanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



order

L23 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1961:60865 CAPLUS Full-text

DOCUMENT NUMBER: 55:60865

ORIGINAL REFERENCE NO.: 55:11652a-d

TITLE: Thioxanthines with potent bronchodilator and coronary dilator properties

AUTHOR(S): Armitage, A. K.; Boswood, Janet; Large, B. J.

CORPORATE SOURCE: May and Baker, Dagenham, UK

SOURCE: British Journal of Pharmacology and Chemotherapy
(1961), 16, 59-76

CODEN: BJPCAL; ISSN: 0366-0826

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

AB The pharmacol. properties of 2 new compds., choline 6-thiotheophyllinate (I) and the choline salt of 3-isobutyl-1-methyl-6-thioxanthine (M & B, 5924) (II) are described. As bronchodilators on the isolated guinea pig tracheal ring preparation, I and II were 57 and 5 times, resp., more active than choline theophyllinate (III). In protective effect against bronchioconstrictor aerosols, III (50 and 100 mg./kg., i.p.) was almost identical with that of I. II (100 mg./kg. orally) appeared to give more protection than III (200 mg./kg.). I and II had very little antihistaminic and antiacetylcholine activity. In cardiovascular studies on the anesthetized cats and dogs, all 3 compds. caused a transient fall in blood pressure. I and II were more potent than III as coronary dilators on the dog heart-lung preparation. As diuretics they were less potent. In doses up to 20 mg./kg., III increased the voluntary locomotor activity of mice. A 50% increase was produced by 12 mg. of I and II each/kg. However, other doses from 5 to 80 mg./kg. either decreased motor

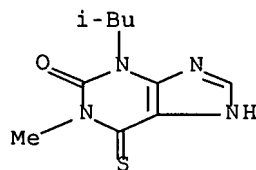
activity or had no effect. A 50% decrease in motor activity was produced by 32 mg. I/kg. and by 30 mg. II/kg. Toxic doses of III caused intense excitement and convulsions, whereas toxic doses of the thioxanthines caused sedation. Death in all cases was due to respiratory failure. In dogs, I in doses as high as 120 mg./kg., orally, caused no ill effects; II at 60 and 80 mg./kg. caused vomiting and retching lasting for about 1 h. II given i.v. to dogs in doses up to 3 mg./kg. caused vomiting, retching, excitation, and restlessness in contrast to the sedation seen in mice.

IT 857018-10-1, Xanthine, 3-isobutyl-1-methyl-6-thio-, compound with
choline
(pharmacol. of)
RN 857018-10-1 CAPLUS
CN Xanthine, 3-isobutyl-1-methyl-6-thio-, compd. with choline (6CI) (CA
INDEX NAME)

CM 1

CRN 42458-91-3

CMF C10 H14 N4 O S



CM 2

CRN 62-49-7

CMF C5 H14 N O

Me₃N—CH₂—CH₂—OH

L23 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1961:56289 CAPLUS Full-text

DOCUMENT NUMBER: 55:56289

ORIGINAL REFERENCE NO.: 55:10804b-d

TITLE: 1,3-Dialkyl-6-thioxanthines: a new series of
bronchodilators and coronary vasodilators

AUTHOR(S): Armitage, A. K.; Wooldridge, K. R. H.

CORPORATE SOURCE: May & Baker, Ltd., Dagenham, UK

SOURCE: Nature (London, United Kingdom) (1960), 188, 1107-8

CODEN: NATUAS; ISSN: 0028-0836

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

AB Thioxanthines were prepared from the corresponding xanthines by refluxing for several hrs. with P2S5 in pyridine. Thionation occurred in the 6-position only. The choline salt of 3-isobutyl-1-methyl-6-thioxanthine (I), the most

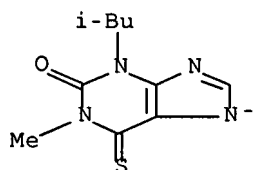
active derivative in vitro for relaxation of the bronchial muscle and dilation of the coronary vessels, is pale-yellow, crystalline, solid, m. 145-7°, and >50% soluble in H₂O at 20°. Choline 6-thiotheophyllinate (II), m. 146-9°, has similar solubility. The thio derivs. are more active in vitro than in vivo. I is more active than II in dilating the coronary vessels of the dog heart-lung preparation or of the anesthetized dog, and in dilating the vessels of the hind leg of the dog perfused with heparinized blood.

IT 97406-00-3, Xanthine, 3-isobutyl-1-methyl-6-thio-, choline salt
(as bronchodilators and coronary vasodilators)
RN 97406-00-3 CAPLUS
CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

CM 1

CRN 97405-99-7

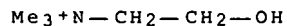
CMF C10 H13 N4 O S



CM 2

CRN 62-49-7

CMF C5 H14 N O



L23 ANSWER 19 OF 22 CAOLD COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: CA58:8327b CAOLD

TITLE: effects of simple liquids on the phagocytic properties of peritoneal macrophages - (I) stimulatory effects of glyceryl trioleate

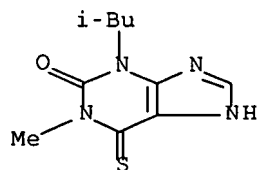
AUTHOR NAME: Cooper, George N.; West, D.

INDEX TERM: 42458-91-3

IT 42458-91-3

RN 42458-91-3 CAOLD

CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



L23 ANSWER 20 OF 22 CAOLD COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: CA57:5924h CAOLD

TITLE: synthesis of some 6-thioxanthines

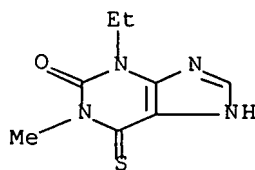
AUTHOR NAME: Wooldridge, Kenneth R. H.; Slack, R.

INDEX TERM: 2006-51-1 2398-70-1 3120-52-3 6501-95-7
 6501-96-8 6603-63-0 13182-58-6 38759-03-4
 38759-27-2 40915-18-2 42458-87-7
 42458-88-8 42458-89-9 42458-90-2
 42458-91-3 42458-92-4 42458-93-5 42458-94-6
 42458-95-7 42458-96-8 42458-97-9 42458-98-0
 42458-99-1 42459-00-7 42459-01-8 42459-02-9
 42459-03-0 42459-04-1 42459-06-3 42459-07-4
 42459-09-6 42459-10-9 63908-37-2 89620-34-8
 90230-11-8 92985-74-5 93263-24-2 93967-36-3
 94625-34-0 94733-92-3 94733-93-4 94733-95-6
 94733-96-7 94763-87-8 96313-21-2 96535-23-8
 96536-20-8 96536-21-9 96635-06-2 96652-89-0
 96654-24-9 96986-49-1 97212-72-1 97282-72-9
 97406-00-3 97406-02-5 97439-87-7 97556-86-0
 97616-67-6 97767-38-9 97767-40-3 97769-20-5
 97783-97-6 98174-21-1 98801-33-3 99688-81-0
 106802-46-4

IT 42458-87-7 42458-88-8 42458-91-3
 42458-96-8 93263-24-2 94733-95-6
 96536-20-8 97212-72-1 97406-00-3
 98174-21-1

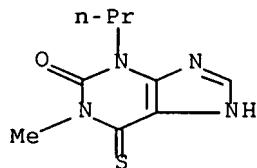
RN 42458-87-7 CAOLD

CN 2H-Purin-2-one, 3-ethyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA INDEX NAME)

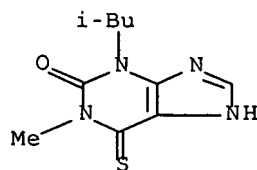


RN 42458-88-8 CAOLD

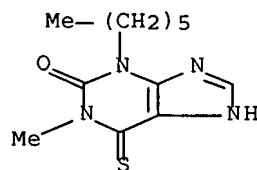
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-propyl-6-thioxo- (9CI) (CA INDEX NAME)



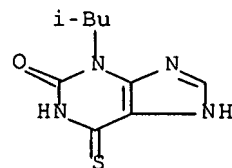
RN 42458-91-3 CAOLD
CN 2H-Purin-2-one, 1,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-6-thioxo- (9CI) (CA INDEX NAME)



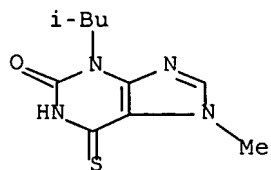
RN 42458-96-8 CAOLD
CN 2H-Purin-2-one, 3-hexyl-1,3,6,7-tetrahydro-1-methyl-6-thioxo- (9CI) (CA INDEX NAME)



RN 93263-24-2 CAOLD
CN Xanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



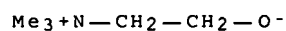
RN 94733-95-6 CAOLD
CN Heteroxanthine, 3-isobutyl-6-thio- (7CI) (CA INDEX NAME)



RN 96536-20-8 CAOLD
CN Choline, compd. with 3-ethyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

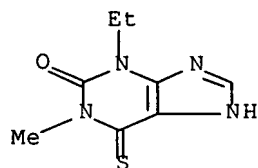
CM 1

CRN 44519-34-8
CMF C5 H13 N O



CM 2

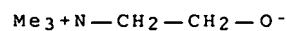
CRN 42458-87-7
CMF C8 H10 N4 O S



RN 97212-72-1 CAOLD
CN Choline, compd. with 1-methyl-3-propyl-6-thioxanthine (7CI) (CA INDEX NAME)

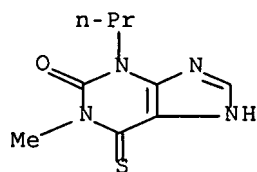
CM 1

CRN 44519-34-8
CMF C5 H13 N O



CM 2

CRN 42458-88-8
CMF C9 H12 N4 O S

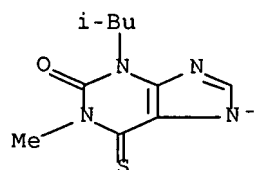


RN 97406-00-3 CAOLD
CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

CM 1

CRN 97405-99-7

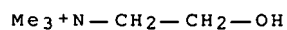
CMF C10 H13 N4 O S



CM 2

CRN 62-49-7

CMF C5 H14 N O

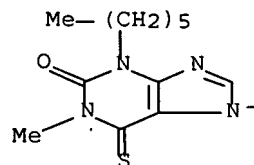


RN 98174-21-1 CAOLD
CN Choline, compd. with 3-hexyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

CM 1

CRN 98174-20-0

CMF C12 H17 N4 O S



CM 2

CRN 62-49-7
CMF C5 H14 N O

Me₃N—CH₂—CH₂—OH

L23 ANSWER 21 OF 22 CAOLD COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: CA56:7935c CAOLD

TITLE: structure-activity relations in a series of 6-thioxanthines
with bronchodilator and coronary dilator properties

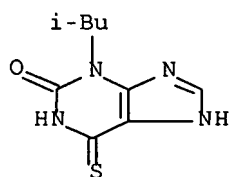
AUTHOR NAME: Armitage, Alan K.; Boswood, J.; Large, B. J.

INDEX TERM: 69-22-7 13182-58-6 56553-57-2 60725-48-6
77038-98-3 90117-29-6 90117-31-0 90230-11-8
92985-74-5 93114-21-7 93114-22-8 93262-67-0
93967-36-3 94031-71-7 94031-72-8 94072-68-1
94072-69-2 94733-92-3 95172-83-1 95172-89-7
95296-03-0 95324-23-5 95348-37-1 96313-22-3
96536-20-8 96536-21-9 96652-89-0 96955-54-3
96986-49-1 97194-78-0 97212-71-0 97212-72-1
97282-72-9 97406-00-3 97406-02-5 97439-87-7
97439-89-9 97616-67-6 97767-38-9 97767-40-3
97769-20-5 97783-97-6 98174-21-1 98801-33-3
99688-81-0 106802-46-4

IT 93114-21-7 94072-69-2 96536-20-8
97212-72-1 97406-00-3 98174-21-1

RN 93114-21-7 CAOLD

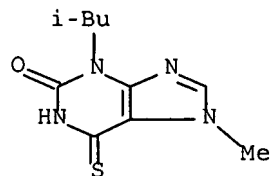
CN Xanthine, 3-isobutyl-6-thio-, sodium deriv. (7CI) (CA INDEX NAME)



● Na

RN 94072-69-2 CAOLD

CN Heteroxanthine, 3-isobutyl-6-thio-, sodium deriv. (7CI) (CA INDEX NAME)



● Na

RN 96536-20-8 CAOLD
CN Choline, compd. with 3-ethyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

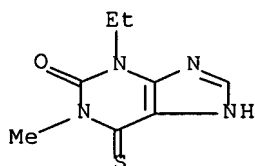
CM 1

CRN 44519-34-8
CMF C5 H13 N O

$\text{Me}_3\text{N}-\text{CH}_2-\text{CH}_2-\text{O}^-$

CM 2

CRN 42458-87-7
CMF C8 H10 N4 O S



RN 97212-72-1 CAOLD
CN Choline, compd. with 1-methyl-3-propyl-6-thioxanthine (7CI) (CA INDEX NAME)

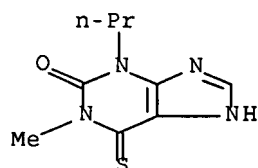
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CRN 44519-34-8
CMF C5 H13 N O

$\text{Me}_3\text{N}-\text{CH}_2-\text{CH}_2-\text{O}^-$

CM 2

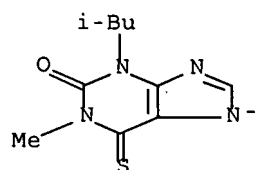
CRN 42458-88-8
CMF C9 H12 N4 O S



RN 97406-00-3 CAOLD
CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

CM 1

CRN 97405-99-7
CMF C10 H13 N4 O S



CM 2

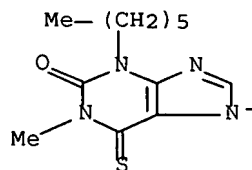
CRN 62-49-7
CMF C5 H14 N O

$\text{Me}_3\text{N}-\text{CH}_2-\text{CH}_2-\text{OH}$

RN 98174-21-1 CAOLD
CN Choline, compd. with 3-hexyl-1-methyl-6-thioxanthine (7CI) (CA INDEX NAME)

CM 1

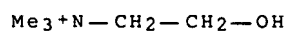
CRN 98174-20-0
CMF C12 H17 N4 O S



CM 2

CRN 62-49-7

CMF C5 H14 N O



L23 ANSWER 22 OF 22 CAOLD COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: CA55:11652a CAOLD

TITLE: thioxanthines with potent bronchodilator and coronary dilator properties

AUTHOR NAME: Armitage, Alan K.; Boswood, J.; Large, B. J.

INDEX TERM: 90230-11-8 97406-00-3

IT 97406-00-3

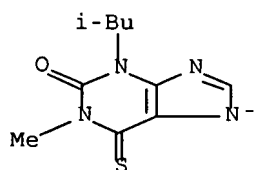
RN 97406-00-3 CAOLD

CN Choline, compd. with 3-isobutyl-1-methyl-6-thioxanthine (6CI, 7CI) (CA INDEX NAME)

CM 1

CRN 97405-99-7

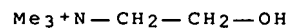
CMF C10 H13 N4 O S



CM 2

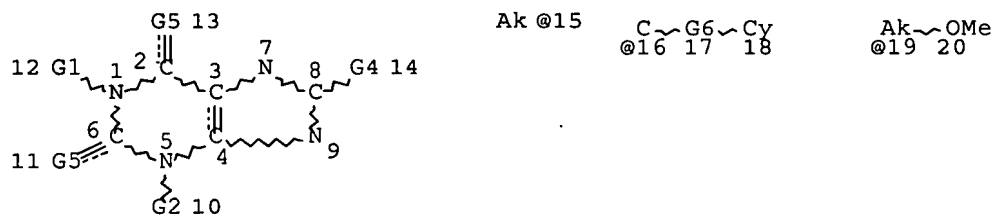
CRN 62-49-7

CMF C5 H14 N O



SEARCH HISTORY

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L1 STR



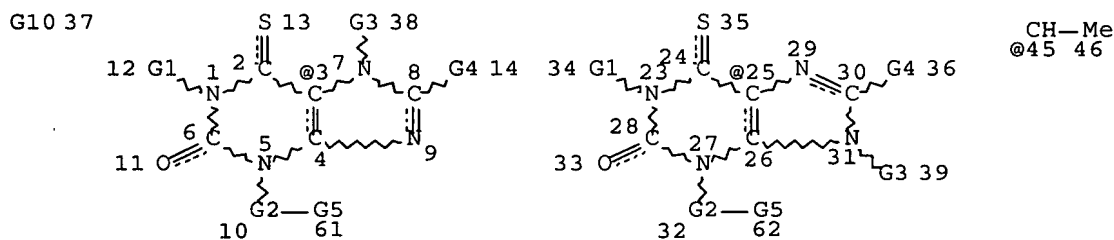
Ak~OEt
@21 22

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VAR G2=16/15/OME/OET/19/21
VAR G4=H/AK
VAR G5=O/S
REP G6=(0-5) C
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 15
CONNECT IS E2 RC AT 19
CONNECT IS E2 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

L4 17287 SEA FILE=REGISTRY SSS FUL L1
L16 STR



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42 @43 44

CH2-Me
@47 48

49 Me-CH-Me 51 52 Me-CH-Ak 54
@50 @53

CH2-Ak
@63 64

65
Me
Me-C-Me
55 @56 57

66
Me
Me-C-Ak
58 @59 60

VAR G1=H/ME
VAR G2=CH2/45/43
VAR G3=H/ME
VAR G4=H/ME/ET
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VAR G10=3/25

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M2-X3 C AT 54
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GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE

L19 23 SEA FILE=REGISTRY SUB=L4 SSS FUL L16

100.0% PROCESSED 263 ITERATIONS

23 ANSWERS

SEARCH TIME: 00.00.01

(FILE 'HOME' ENTERED AT 16:04:30 ON 12 APR 2007)

FILE 'REGISTRY' ENTERED AT 16:04:37 ON 12 APR 2007

L1 STR
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L3 115605 SEA SSS FUL L1 EXTEND
L4 17287 SEA SSS FUL L1
SAVE TEMP L4 BER537FULL/A
L5 STR L1
L6 1 SEA SUB=L4 SSS SAM L5
D SCAN
L7 229 SEA SUB=L4 SSS FUL L5 EXTEND
L8 17 SEA SUB=L4 SSS FUL L5
SAVE TEMP L8 BER537FULA/A

FILE 'REGISTRY' ENTERED AT 16:17:11 ON 12 APR 2007
D STAT QUE L8

FILE 'CAPLUS' ENTERED AT 16:17:15 ON 12 APR 2007

L9 8 SEA ABB=ON L8
D IBIB ED ABS HITSTR 1-8

FILE 'HOME' ENTERED AT 16:17:29 ON 12 APR 2007

D STAT QUE L8
D COST

FILE 'REGISTRY' ENTERED AT 16:18:23 ON 12 APR 2007

L10 STR L5
L11 1 SEA SUB=L4 SSS SAM L10

D SCAN
L12 52 SEA SUB=L4 SSS FUL L10 EXTEND
L13 6 SEA SUB=L4 SSS FUL L10
SAVE TEMP L13 BER537FULB/A

FILE 'REGISTRY' ENTERED AT 16:27:53 ON 12 APR 2007
D STAT QUE L13

FILE 'CAPLUS' ENTERED AT 16:27:53 ON 12 APR 2007
L14 4 SEA ABB=ON L13
D IBIB ED ABS HITSTR L14 1-4

FILE 'HOME' ENTERED AT 16:28:06 ON 12 APR 2007
D STAT QUE L13
D COST

FILE 'STNGUIDE' ENTERED AT 16:28:33 ON 12 APR 2007

FILE 'REGISTRY' ENTERED AT 16:30:19 ON 12 APR 2007
L15 STR L5
L16 STR L10
L17 3 SEA SUB=L4 SSS SAM L16
D SCAN
L18 263 SEA SUB=L4 SSS FUL L16 EXTEND
L19 23 SEA SUB=L4 SSS FUL L16
SAVE TEMP L19 BER537FULC/A
L20 ANALYZE L19 1- LC : 7 TERMS
D

FILE 'REGISTRY' ENTERED AT 16:37:19 ON 12 APR 2007
D STAT QUE L19

FILE 'CAPLUS' ENTERED AT 16:37:19 ON 12 APR 2007
L21 18 SEA ABB=ON L19

FILE 'CAOLD' ENTERED AT 16:37:20 ON 12 APR 2007
L22 4 SEA ABB=ON L19

FILE 'CAPLUS, CAOLD' ENTERED AT 16:37:27 ON 12 APR 2007
L23 22 DUP REM L21 L22 (0 DUPLICATES REMOVED)
ANSWERS '1-18' FROM FILE CAPLUS
ANSWERS '19-22' FROM FILE CAOLD
D IBIB ED ABS HITSTR 1-18
D IALL HITSTR 19-22

FILE 'HOME' ENTERED AT 16:38:01 ON 12 APR 2007
D STAT QUE L19

=>

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4-563

ACCESS DB # 221706
PLEASE PRINT CLEARLY

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: MARK BERCH Examiner #: 59193 Date: 4/13/02
 Art Unit: 1624 Phone Number: 2-0663 Serial Number: 10511537B
 Location (Bldg/Room#): 5C01 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following: ME

Title of Invention: _____

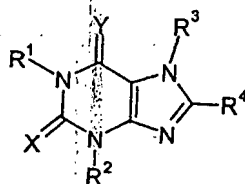
Inventors (please provide full names): _____

Earliest Priority Date: _____

Search Topic:

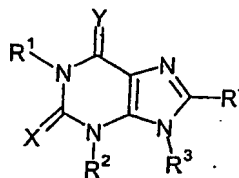
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



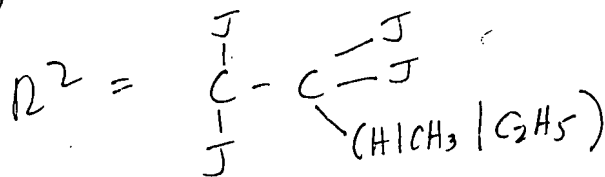
(Ia)

or



(Ib)

X=Y=S

all J, R¹ = R³ = R⁴ = H/CH₃

20070412-10511537-2

STAFF USE ONLY

Searcher: POURB

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 4-12-02Searcher Prep & Review Time: 20Online Time: 11

Type of Search

____ NA Sequence (#)

____ AA Sequence (#)

2 Structure (#)

____ Bibliographic

____ Litigation

____ Fulltext

____ Other

Vendors and cost where applicable

71 STN _____ Dialog

____ Questel/Orbit _____ Lexis/Nexis

____ Westlaw _____ WWW/Internet

____ In-house sequence systems

____ Commercial _____ Oligomer _____ Score/Length
 ____ Interference _____ SPDI _____ Encode/Transl
 ____ Other (specify)

=> fil reg; d stat que l13; fil capl; s l13
FILE 'REGISTRY' ENTERED AT 16:27:53 ON 12 APR 2007
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 11 APR 2007 HIGHEST RN 929721-97-1
DICTIONARY FILE UPDATES: 11 APR 2007 HIGHEST RN 929721-97-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

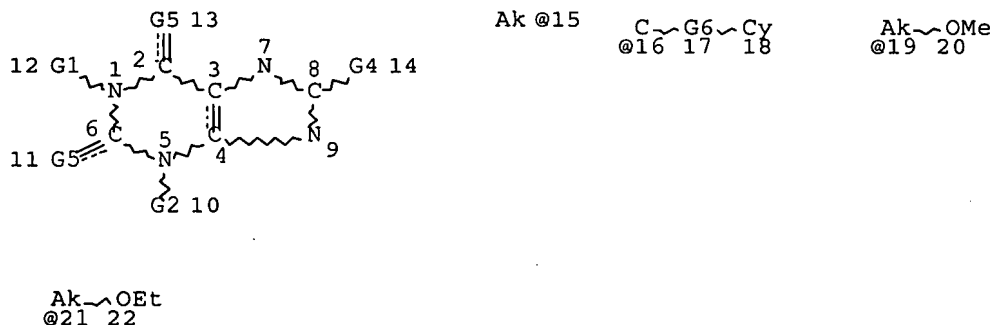
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

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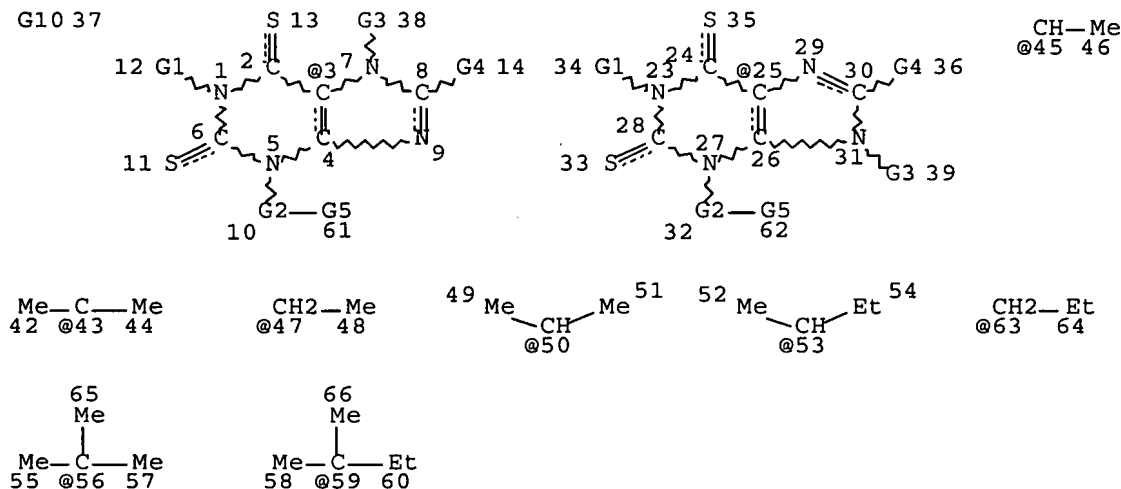


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VAR G4=H/AK
VAR G5=O/S
REP G6=(0-5) C
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 15
CONNECT IS E2 RC AT 19
CONNECT IS E2 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

L4 17287 SEA FILE=REGISTRY SSS FUL L1
L10 STR



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VAR G5=ME/47/63/50/53/56/59
VAR G10=3/25

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE

L13 6 SEA FILE=REGISTRY SUB=L4 SSS FUL L10

100.0% PROCESSED 52 ITERATIONS

SEARCH TIME: 00.00.01

6 ANSWERS

FILE 'CAPLUS' ENTERED AT 16:27:53 ON 12 APR 2007

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FILE COVERS 1907 - 12 Apr 2007 VOL 146 ISS 16
FILE LAST UPDATED: 11 Apr 2007 (20070411/ED)

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<http://www.cas.org/infopolicy.html>
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L14 4 L13

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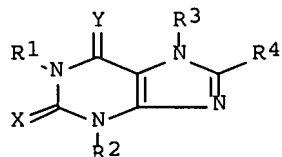
L14 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:855927 CAPLUS Full-text
DOCUMENT NUMBER: 139:350580
TITLE: Preparation of xanthinethione derivatives as
myeloperoxidase inhibitors
INVENTOR(S): Hanson, Sverker; Nordvall, Gunnar; Tiden, Anna-Karin
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003089430 | A1 | 20031030 | WO 2003-SE617 | 20030415 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2480452 | A1 | 20031030 | CA 2003-2480452 | 20030415 |
| AU 2003224548 | A1 | 20031103 | AU 2003-224548 | 20030415 |
| EP 1499613 | A1 | 20050126 | EP 2003-721211 | 20030415 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003009012 | A | 20050201 | BR 2003-9012 | 20030415 |
| CN 1646531 | A | 20050727 | CN 2003-808355 | 20030415 |
| JP 2005526836 | T | 20050908 | JP 2003-586151 | 20030415 |
| NZ 535406 | A | 20060831 | NZ 2003-535406 | 20030415 |
| ZA 2004007815 | A | 20051004 | ZA 2004-7815 | 20040928 |
| US 2005234036 | A1 | 20051020 | US 2004-511537 | 20041015 |
| NO 2004004998 | A | 20050118 | NO 2004-4998 | 20041117 |
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| | | | SE 2002-2239 | A 20020717 |

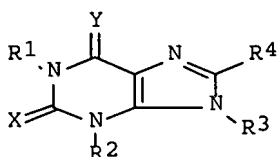
WO 2003-SE617

W 20030415

OTHER SOURCE(S): MARPAT 139:350580
ED Entered STN: 31 Oct 2003
GI



I



II

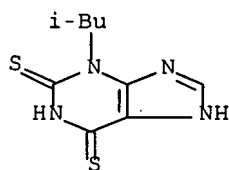
AB Xanthinethiones I and II [one of X and Y = S, the other = O, S; R1, R3, R4 = H, alkyl; R2 = H, (un)substituted alkyl] were prepared for use as myeloperoxidase (MPO) inhibitors in the treatment of neuroinflammatory disorders. Thus, Me2CHCH2NHCSNH2 was cyclized with NCCH2CO2Et to give 6-amino-1-isobutyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one which was nitrosated, reduced to the 5,6-diamine, and cyclized with HCO2H to give II [R1, R3, R4 = H, R2 = CH2CHMe2, X = S, Y = O]. This compound had IC50 for inhibition of MPO of 0.87 μM.

IT 618913-17-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

RN 618913-17-0 CAPLUS

CN 1H-Purine-2,6-dithione, 3,7-dihydro-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:502824 CAPLUS Full-text
DOCUMENT NUMBER: 137:63122

TITLE: Preparation of purine derivatives or therapeutic use as phosphodiesterase IV inhibitors

INVENTOR(S): Chasin, Mark; Cavalla, David J.; Hofer, Peter; Gehrig, Andre; Wintergerst, Peter

PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg

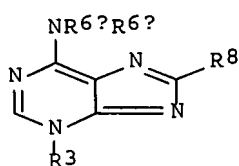
SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 285,473.
CODEN: USXXAM

DOCUMENT TYPE: Patent

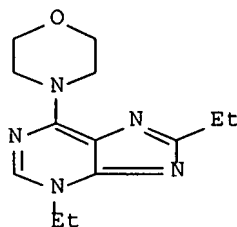
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

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|------------------------|------|----------|-----------------|-------------|
| US 6413975 | B1 | 20020702 | US 2000-539571 | 20000331 |
| IN 180930 | A1 | 19980404 | IN 1995-CA1508 | 19951123 |
| IN 181538 | A1 | 19980711 | IN 1995-CA1506 | 19951123 |
| HU 200200938 | A2 | 20021028 | HU 2002-938 | 20000331 |
| JP 2001316314 | A | 20011113 | JP 2000-136383 | 20000509 |
| US 2003073834 | A1 | 20030417 | US 2002-62280 | 20020201 |
| PRIORITY APPLN. INFO.: | | | US 1999-285473 | A2 19990402 |
| | | | IN 1994-CA514 | A1 19940630 |
| | | | US 1997-963054 | A2 19971103 |
| | | | US 1997-875487 | A2 19971113 |
| | | | US 1998-151949 | A2 19980911 |
| | | | US 1998-210556 | A2 19981211 |
| | | | US 1998-210557 | A2 19981211 |
| | | | US 1999-227057 | A2 19990107 |
| | | | US 1999-237638 | A2 19990126 |
| | | | US 1999-361196 | A2 19990726 |
| | | | US 2000-506624 | A2 20000218 |
| | | | US 2000-539571 | A2 20000331 |
| | | | US 2000-547575 | A2 20000412 |
| | | | US 2000-547898 | A2 20000412 |
| | | | US 2000-636146 | A2 20000810 |
| | | | US 2000-724321 | B1 20001128 |

OTHER SOURCE(S): MARPAT 137:63122
ED Entered STN: 04 Jul 2002
GI



I



II

AB Purines, such as I [R3, R6a, R6b, R8 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, etc.], were prepared for pharmaceutical use as phosphodiesterase IV (PDE IV) inhibitors. Thus, 3,8-diethyl-6-morpholino- 3H-purine (II) was prepared by conversion of 3,8-diethyl-2-thioxanthine to 3,8-diethylhypoxanthine using 2N NaOH and nickel aluminum alloy, reaction of 3,8-diethylhypoxanthine to 3,8-diethyl-6-thiohypoxanthine using phosphorus pentasulfide in pyridine and, finally, reaction of 3,8-diethyl-6-thiohypoxanthine with morpholine. The prepared purine derivs. were assayed for PDE IV inhibition.

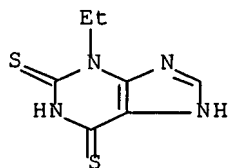
IT 162278-87-7P 162278-88-8P 162278-90-2P
439694-45-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of purine derivs. for therapeutic use as phosphodiesterase IV
inhibitors)

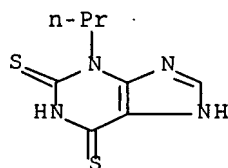
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CN 1H-Purine-2,6-dithione, 3-ethyl-3,7-dihydro- (9CI) (CA INDEX NAME)



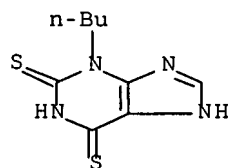
RN 162278-88-8 CAPLUS

CN 1H-Purine-2,6-dithione, 3,7-dihydro-3-propyl- (9CI) (CA INDEX NAME)



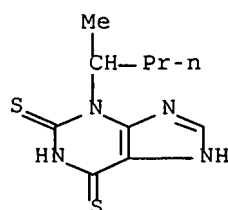
RN 162278-90-2 CAPLUS

CN 1H-Purine-2,6-dithione, 3-butyl-3,7-dihydro- (9CI) (CA INDEX NAME)



RN 439694-45-8 CAPLUS

CN 1H-Purine-2,6-dithione, 3,7-dihydro-3-(1-methylbutyl)- (9CI) (CA INDEX NAME)

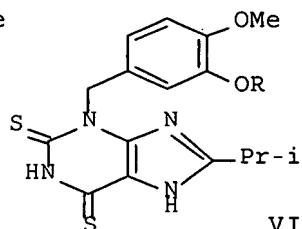
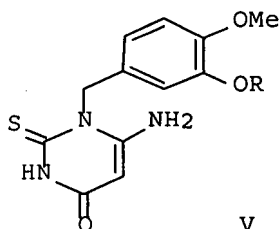
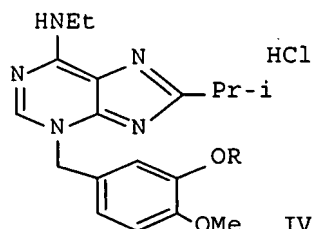
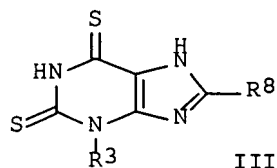
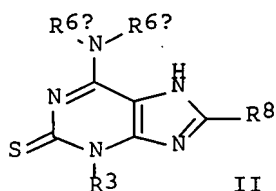
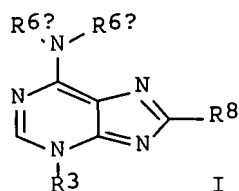


REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:725418 CAPLUS Full-text
DOCUMENT NUMBER: 133:296324
TITLE: Synthesis and phosphodiesterase IV inhibition activity
of purine derivatives
INVENTOR(S): Chasin, Mark; Cavalla, David; Hofer, Peter; Gehrig,
Andre; Wintergest, Peter
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2000059449 | A2 | 20001012 | WO 2000-US8525 | 20000331 |
| WO 2000059449 | A3 | 20010104 | | |
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| IN 180930 | A1 | 19980404 | IN 1995-CA1508 | 19951123 |
| IN 181538 | A1 | 19980711 | IN 1995-CA1506 | 19951123 |
| CA 2367143 | A1 | 20001012 | CA 2000-2367143 | 20000331 |
| EP 1169321 | A2 | 20020109 | EP 2000-919929 | 20000331 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| HU 200200938 | A2 | 20021028 | HU 2002-938 | 20000331 |
| JP 2002541078 | T | 20021203 | JP 2000-609014 | 20000331 |
| BR 2000011182 | A | 20030610 | BR 2000-11182 | 20000331 |
| JP 2001316314 | A | 20011113 | JP 2000-136383 | 20000509 |
| PRIORITY APPLN. INFO.: | | | US 1999-285473 | A 19990402 |
| | | | IN 1994-CA514 | A1 19940630 |
| | | | WO 2000-US8525 | W 20000331 |

OTHER SOURCE(S): MARPAT 133:296324
ED Entered STN: 13 Oct 2000
GI



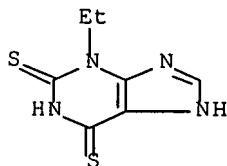
AB The purine (I) (R3, R8, R6a, R6b = H, (un)substituted alkyl, alkenyl, cycloalkyl, aryl, heterocyclyl, heteroaryl etc.), thioisoguanine (II), dithioxanthine (III) derivs., and their pharmaceutically accepted salts were synthesized. Thus, purine (IV; R = (CH2)5) was prepared by etherification of isovanilline with cyclopentanol, oximation, reduction to amine, conversion to isothiocyanate, amination to thiourea followed by heterocyclization with Et cyanoacetate to thiouracil (V). V was nitrosylated, reduced, reacted with isobutyric anhydride to give isobutyrylamine which on treatment with phosphorus pentasulfide gave dithioxanthine (VI). VI, in a pressure reactor gave purine-2-thione which was reduced with Raney-nickel to give IV. The IC50 of IV against phosphodiesterase IV inhibition was 0.32 μ M. I, II and III were effective in effecting PDE IV inhibition in patients in need thereof.

IT 162278-87-7P 162278-88-8P 162278-90-2P
300783-45-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of purine derivs. as phosphodiesterase IV inhibitors)

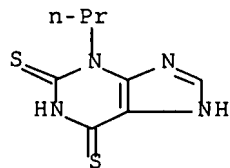
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CN 1H-Purine-2,6-dithione, 3-ethyl-3,7-dihydro- (9CI) (CA INDEX NAME)

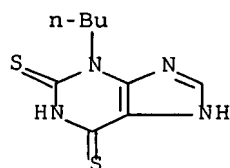


RN 162278-88-8 CAPLUS

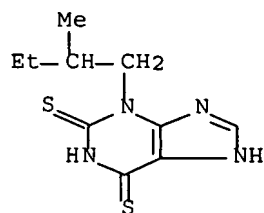
CN 1H-Purine-2,6-dithione, 3,7-dihydro-3-propyl- (9CI) (CA INDEX NAME)



RN 162278-90-2 CAPLUS
CN 1H-Purine-2,6-dithione, 3-butyl-3,7-dihydro- (9CI) (CA INDEX NAME)



RN 300783-45-3 CAPLUS
CN 1H-Purine-2,6-dithione, 3,7-dihydro-3-(2-methylbutyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:492020 CAPLUS Full-text
DOCUMENT NUMBER: 122:239459
TITLE: Preparation of purines, isoguanines, and dithioxanthines as phosphodiesterase-IV inhibitors
INVENTOR(S): Cavalla, David; Hofer, Peter; Gehrig, Anddre; Wintergest, Peter
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

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| WO 9500516 | A1 | 19950105 | WO 1994-GB1334 | 19940621 |
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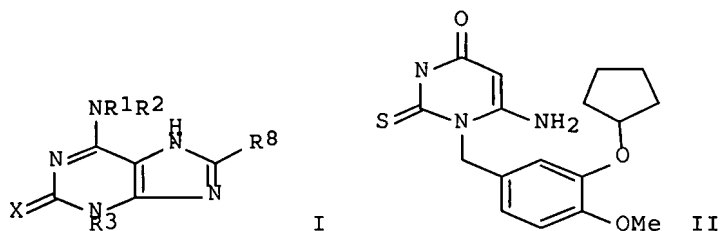
NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

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| CA 2165433 | A1 | 19941223 | CA 1994-2165433 | 19940621 |
| CA 2165433 | C | 20020528 | | |
| AU 9469771 | A | 19950117 | AU 1994-69771 | 19940621 |
| AU 683270 | B2 | 19971106 | | |
| EP 705265 | A1 | 19960410 | EP 1994-918456 | 19940621 |
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| CN 1125445 | A | 19960626 | CN 1994-192521 | 19940621 |
| CN 1045778 | B | 19991020 | | |
| HU 74176 | A2 | 19961128 | HU 1995-3545 | 19940621 |
| JP 09500376 | T | 19970114 | JP 1995-502570 | 19940621 |
| JP 3350550 | B2 | 20021125 | | |
| EP 916672 | A1 | 19990519 | EP 1999-100735 | 19940621 |
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| EP 916673 | A1 | 19990519 | EP 1999-100736 | 19940621 |
| EP 916673 | B1 | 20030129 | | |
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| AT 182593 | T | 19990815 | AT 1994-918456 | 19940621 |
| ES 2137371 | T3 | 19991216 | ES 1994-918456 | 19940621 |
| NZ 328914 | A | 20000825 | NZ 1994-328914 | 19940621 |
| AT 231863 | T | 20030215 | AT 1999-100736 | 19940621 |
| ZA 9404463 | A | 19950217 | ZA 1994-4463 | 19940622 |
| IN 177888 | A1 | 19970222 | IN 1994-CA514 | 19940630 |
| TW 418208 | B | 20010111 | TW 1994-83107047 | 19940802 |
| IN 180930 | A1 | 19980404 | IN 1995-CA1508 | 19951123 |
| IN 181538 | A1 | 19980711 | IN 1995-CA1506 | 19951123 |
| FI 9506168 | A | 19960201 | FI 1995-6168 | 19951221 |
| NO 9505219 | A | 19960222 | NO 1995-5219 | 19951221 |
| BG 62933 | B1 | 20001130 | BG 1995-100258 | 19951227 |
| US 5939422 | A | 19990817 | US 1996-578580 | 19960408 |
| US 6310205 | B1 | 20011030 | US 1999-237638 | 19990126 |
| US 6294541 | B1 | 20010925 | US 1999-418330 | 19991014 |
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PRIORITY APPLN. INFO.:

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| GB 1993-12853 | A | 19930622 |
| EP 1994-918456 | A3 | 19940621 |
| NZ 1994-267468 | A1 | 19940621 |
| WO 1994-GB1334 | W | 19940621 |
| IN 1994-CA514 | A1 | 19940630 |
| US 1996-578580 | A2 | 19960408 |
| US 1996-659767 | A1 | 19960606 |
| US 1997-69371P | P | 19971212 |
| US 1998-200615 | B2 | 19981130 |
| US 1998-210556 | A2 | 19981211 |
| US 1999-285473 | A1 | 19990402 |

OTHER SOURCE(S): MARPAT 122:239459
ED Entered STN: 18 Apr 1995
GI



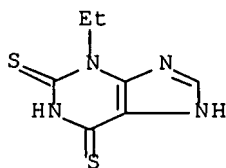
AB Title compds. [e.g., I; R1-R3, R8 = H, (cyclo)alkyl, (hetero)aryl, etc.; NR1R2 = heterocyclyl] were prepared. Title compds. have bronchial and tracheal relaxation and/or antiinflammatory activity. Thus, isovanillin was converted in 5 steps to 3,4-(HO)(MeO)C6H3CH2NHCSNH2 which was cyclocondensed with NCCH2CO2Et to give thiouracil II. The latter was converted in 3 steps to 6-amino-1-(3-cyclopentyloxy-4-methoxybenzyl)-5-isobutyrylamino-2-thiouracil which was cyclized and the product converted in 4 steps to I.HCl (R1 = Et, R2 = H, R3 = 3-cyclopentyloxy-4-methoxybenzyl, R8 = CHMe2) (III). III gave 64% inhibition of ovalbumin-induced bronchoalveolar eosinophil production in guinea pigs at 5mg/kg i.p.

IT 162278-87-7P 162278-88-8P 162278-90-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of purines, isoguanines, and dithioxanthines as phosphodiesterase-IV inhibitors)

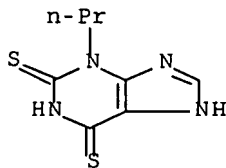
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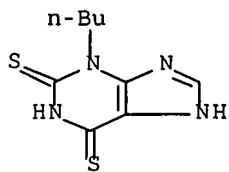
RN 162278-88-8 CAPLUS

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RN 162278-90-2 CAPLUS

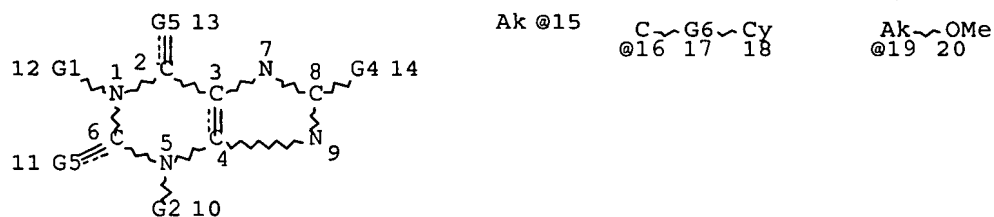
CN 1H-Purine-2,6-dithione, 3-butyl-3,7-dihydro- (9CI) (CA INDEX NAME)



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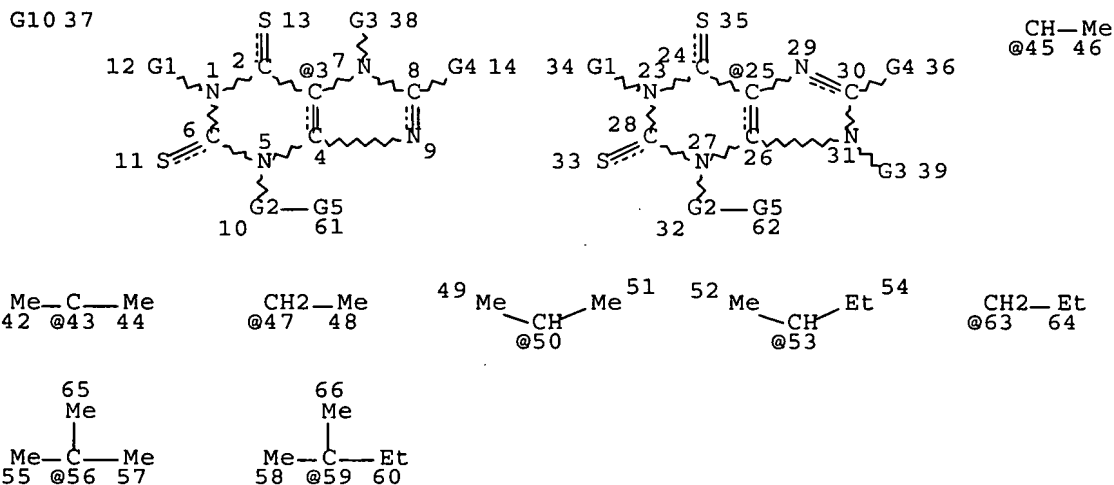


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D STAT QUE L8
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Serial No.: 10/511,537

Author Search

=> FILE CAPLUS

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

Search
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L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:855927 CAPLUS Full-text
DOCUMENT NUMBER: 139:350580
TITLE: Preparation of xanthinethione derivatives as
myeloperoxidase inhibitors
INVENTOR(S): Hanson, Sverker; Nordvall, Gunnar;
Tiden, Anna-Karin
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2003089430 | A1 | 20031030 | WO 2003-SE617 | 20030415 |
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Serial No.: 10/511,537

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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| CA 2480452 | A1 | 20031030 | CA 2003-2480452 | 20030415 |
| AU 2003224548 | A1 | 20031103 | AU 2003-224548 | 20030415 |
| EP 1499613 | A1 | 20050126 | EP 2003-721211 | 20030415 |

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|---------------|----|----------|----------------|----------|
| BR 2003009012 | A | 20050201 | BR 2003-9012 | 20030415 |
| CN 1646531 | A | 20050727 | CN 2003-808355 | 20030415 |
| JP 2005526836 | T | 20050908 | JP 2003-586151 | 20030415 |
| NZ 535406 | A | 20060831 | NZ 2003-535406 | 20030415 |
| ZA 2004007815 | A | 20051004 | ZA 2004-7815 | 20040928 |
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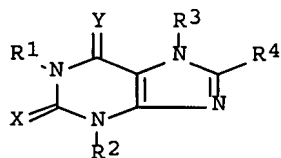
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| SE 2002-1193 | A | 20020419 |
| SE 2002-2239 | A | 20020717 |
| WO 2003-SE617 | W | 20030415 |

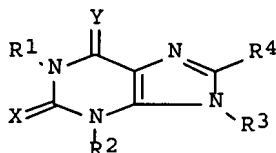
OTHER SOURCE(S): MARPAT 139:350580

ED Entered STN: 31 Oct 2003

GI



I



II

AB Xanthinethiones I and II [one of X and Y = S, the other = O, S; R1, R3, R4 = H, alkyl; R2 = H, (un)substituted alkyl] were prepared for use as myeloperoxidase (MPO) inhibitors in the treatment of neuroinflammatory disorders. Thus, Me2CHCH2NHCSNH2 was cyclized with NCCH2CO2Et to give 6-amino-1-isobutyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one which was nitrosated, reduced to the 5,6-diamine, and cyclized with HCO2H to give II [R1, R3, R4 = H, R2 = CH2CHMe2, X = S, Y = O]. This compound had IC50 for inhibition of MPO of 0.87 μ M.

REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Structure Search

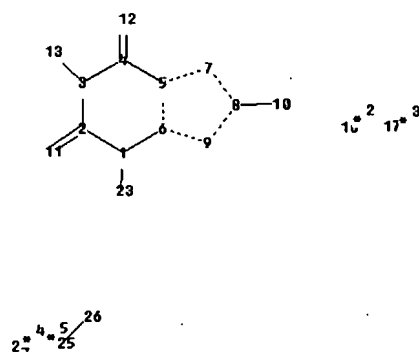
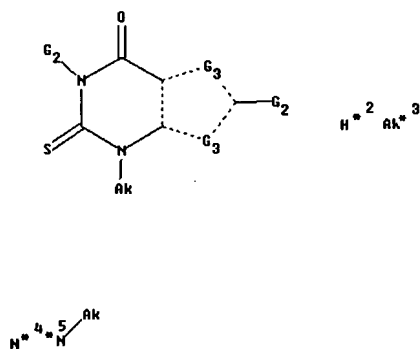
=> D QUE L4

L1

STR

Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



chain nodes :

10 11 12 13 16 17 23 24 25 26

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

1-23 2-11 3-13 4-12 8-10 25-26

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9

exact/norm bonds :

1-2 1-6 1-23 2-3 2-11 3-4 3-13 4-5 4-12 5-6 5-7 6-9 7-8 8-9 8-10 25-26

G1

G2: [*1], [*2]

G3: [*3], [*4]

Connectivity :

11:1 E exact RC ring/chain 17:1 E exact RC ring/chain 23:1 E exact RC ring/chain

24:2 E exact RC ring/chain 26:1 E exact RC ring/chain

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS

11:CLASS 12:CLASS 13:CLASS 16:CLASS 17:CLASS 23:CLASS 24:CLASS 25:CLASS

26:CLASS

Generic attributes :

17:
Saturation : Saturated
23:
Saturation : Saturated
26:
Saturation : Saturated

Element Count :

Node 17: Limited
C,C1-3

Node 26: Limited
C,C1-3

L3 21. SEA FILE=REGISTRY SSS FUL L1
L4 48 SEA FILE=CAPLUS ABB=ON PLU=ON L3

=> S L4 NOT L8
L9 47 L4 NOT L8

=> D IBIB ED ABS HITSTR 1-47

L9 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:205972 CAPLUS Full-text
DOCUMENT NUMBER: 142:176578

TITLE: Product class 17: purines
AUTHOR(S): Seela, F.; Ramzaeva, N.; Rosemeyer, H.
CORPORATE SOURCE: Germany
SOURCE: Science of Synthesis (2004), 16, 945-1108
CODEN: SSCYJ9

PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

ED Entered STN: 15 Mar 2004

AB A review. Methods for preparing purines are reviewed including cyclization, ring transformation, and substituent modification. Oxidation of purines is included.

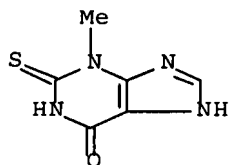
IT 28139-02-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and oxidation of purines via cyclization, ring transformation and substituent modification)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



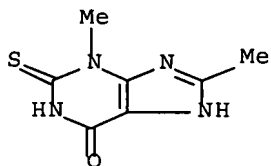
IT 91725-06-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and oxidation of purines via cyclization, ring transformation
and
substituent modification)

RN 91725-06-3 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,8-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 762 THERE ARE 762 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L9 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:706960 CAPLUS Full-text

DOCUMENT NUMBER: 139:230796

TITLE: Synthesis of new purine derivatives

INVENTOR(S): Miyamoto, Kenichi; Sawanishi, Hiroyuki; Suzuki, Koichi; Yamamoto, Manabu; Shimura, Susumu

PATENT ASSIGNEE(S): Lotte Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

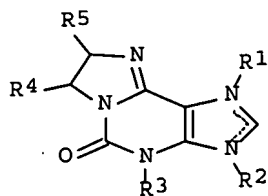
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| JP 2003252875 | A | 20030910 | JP 2002-58098 | 20020304 |
| KR 2003072251 | A | 20030913 | KR 2003-13401 | 20030304 |
| PRIORITY APPLN. INFO.: | | | JP 2002-58098 | A 20020304 |

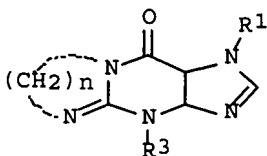
OTHER SOURCE(S): MARPAT 139:230796

ED Entered STN: 10 Sep 2003

GI



I



II

AB The patent relates to the preparation of purine derivs. and salts for pharmaceutical uses such as PDE IV isoenzyme inhibitor. The purine derivs. have the following formula (I) wherein R1, R2, R3 are hydrogen, or hydroxy, low alkyloxy, acyl substituted C1-C6 alkyl, or phenyl; and R4, and R5 are independently hydroxy, low alkyloxy, acyl substituted C1-C6 alkyl, or Ph group; and pharmaceutically compatible salts. The purine derivs. and pharmaceutically compatible salts may have the following formula (II) wherein R1, R2 are hydrogen, or hydroxy, low alkyloxy, acyl substituted C1-C6 alkyl, or phenyl; and n = 2 or 3. Thus, 8-methyl-4-propyl-4,5,7,8-tetrahydro-1H-imidazole-[2,1,i]purine-5-one prepared from 6-[(2-hydroxy-1-methyl)ethyl]amino-3-propylpurine-2-one in presence of triethylamine, and methanesulfonyl chloride was evaluated for PDE I test and gave greater activity than the control using Denoufylline.

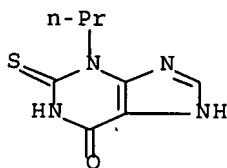
IT 156733-29-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(in preparation of new purine derivs.)

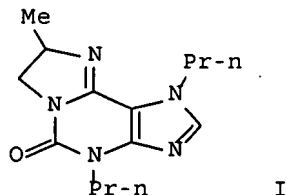
RN 156733-29-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-propyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2002:723414 CAPLUS Full-text
 DOCUMENT NUMBER: 138:137075
 TITLE: Synthesis and cyclic AMP phosphodiesterase 4 isoenzyme inhibitory activity of heterocycle condensed purines
 AUTHOR(S): Suzuki, Hirokazu; Yamamoto, Manabu; Shimura, Susumu; Miyamoto, Ken-ichi; Yamamoto, Kenji; Sawanishi, Hiroyuki
 CORPORATE SOURCE: Department of Synthetic Chemistry, Hokuriku University, Kanazawa, 920-1181, Japan
 SOURCE: Chemical & Pharmaceutical Bulletin (2002), 50(9), 1163-1168
 CODEN: CPBTAL; ISSN: 0009-2363
 PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 138:137075
 ED Entered STN: 24 Sep 2002
 GI



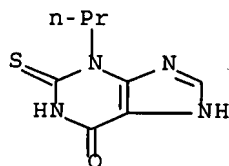
AB To reverse the adverse reactions of alkylxanthines and to develop novel inhibitors of cAMP phosphodiesterase 4 (PDE4), a series of heterocycle [a]-, [b]-, [c,d]-, and [i]-condensed purines were designed and synthesized. Although all compds. did not display PDE1 and PDE3 inhibitory activities, several heterocycle [i]-condensed purines strongly inhibited PDE4. Especially, dl-3,4-dipropyl-8-methyl-4,5,7,8-tetrahydro-1H-imidazo[2,1-i]purin-5-one (I) exhibited comparable PDE4 inhibitory activity (IC₅₀=1.9 μM) to rolipram and denbufylline (DBF).

IT 156733-29-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of heterocycle condensed purines from purine and pyrimidine derivs. and their activity as cAMP phosphodiesterase 4 isoenzyme inhibitors)

RN 156733-29-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-propyl-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:502824 CAPLUS Full-text

DOCUMENT NUMBER: 137:63122

TITLE: Preparation of purine derivatives or therapeutic use as phosphodiesterase IV inhibitors

INVENTOR(S): Chasin, Mark; Cavalla, David J.; Hofer, Peter; Gehrig, Andre; Wintergerst, Peter

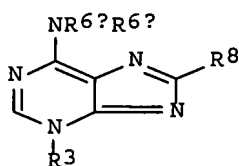
PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg

Serial No.: 10/511,537

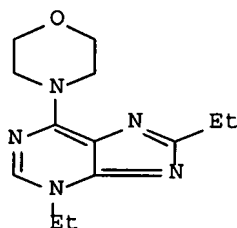
SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 285,473.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 21
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 6413975 | B1 | 20020702 | US 2000-539571 | 20000331 |
| IN 180930 | A1 | 19980404 | IN 1995-CA1508 | 19951123 |
| IN 181538 | A1 | 19980711 | IN 1995-CA1506 | 19951123 |
| HU 200200938 | A2 | 20021028 | HU 2002-938 | 20000331 |
| JP 2001316314 | A | 20011113 | JP 2000-136383 | 20000509 |
| US 2003073834 | A1 | 20030417 | US 2002-62280 | 20020201 |
| PRIORITY APPLN. INFO.: | | | US 1999-285473 | A2 19990402 |
| | | | IN 1994-CA514 | A1 19940630 |
| | | | US 1997-963054 | A2 19971103 |
| | | | US 1997-875487 | A2 19971113 |
| | | | US 1998-151949 | A2 19980911 |
| | | | US 1998-210556 | A2 19981211 |
| | | | US 1998-210557 | A2 19981211 |
| | | | US 1999-227057 | A2 19990107 |
| | | | US 1999-237638 | A2 19990126 |
| | | | US 1999-361196 | A2 19990726 |
| | | | US 2000-506624 | A2 20000218 |
| | | | US 2000-539571 | A2 20000331 |
| | | | US 2000-547575 | A2 20000412 |
| | | | US 2000-547898 | A2 20000412 |
| | | | US 2000-636146 | A2 20000810 |
| | | | US 2000-724321 | B1 20001128 |

OTHER SOURCE(S): MARPAT 137:63122
 ED Entered STN: 04 Jul 2002
 GI



I



II

AB Purines, such as I [R3, R6a, R6b, R8 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, etc.], were prepared for pharmaceutical use as phosphodiesterase IV (PDE IV) inhibitors. Thus, 3,8-diethyl-6-morpholino-3H-purine (II) was prepared by conversion of 3,8-diethyl-2-thioxanthine to 3,8-diethylhypoxanthine using 2N NaOH and nickel aluminum alloy, reaction of 3,8-diethylhypoxanthine to 3,8-diethyl-6-thiohypoxanthine using phosphorus pentasulfide in pyridine and, finally, reaction of 3,8-diethyl-6-

Serial No.: 10/511,537

thiohypoxanthine with morpholine. The prepared purine derivs. were assayed for PDE IV inhibition.

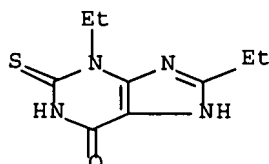
IT 162278-04-8, 3,8-Diethyl-2-thioxanthine

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of purine derivs. for therapeutic use as phosphodiesterase IV inhibitors)

RN 162278-04-8 CAPLUS

CN 6H-Purin-6-one, 3,8-diethyl-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:90055 CAPLUS Full-text

DOCUMENT NUMBER: 136:131252

TITLE: Cationic materials and methods for covalent bonding nucleic acids to high purity silica surfaces

INVENTOR(S): Lyles, Mark B.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 9 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2002008237 | A2 | 20020131 | WO 2001-US23079 | 20010720 |
| WO 2002008237 | A3 | 20021107 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2001076023 | A5 | 20020205 | AU 2001-76023 | 20010720 |
| US 2002103350 | A1 | 20020801 | US 2001-910697 | 20010720 |
| US 6855817 | B2 | 20050215 | | |
| EP 1305328 | A2 | 20030502 | EP 2001-953590 | 20010720 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| US 2005148067 | A1 | 20050707 | US 2005-57440 | 20050214 |
| PRIORITY APPLN. INFO.: | | | US 2000-220096P | P 20000721 |

US 2001-910697
WO 2001-US23079A 20010720
W 20010720

ED Entered STN: 01 Feb 2002

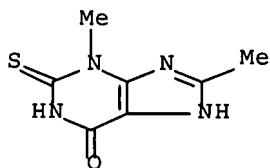
AB Surfaces containing high purity silica (silicon dioxide) exhibit high loading potential for nucleic acids. Formulations containing nucleic acids and materials which mask the electrostatic interactions between the nucleic acids and surfaces are disclosed. By masking the phosphate charges of the nucleic acids, undesired interactions may be minimized or eliminated, thereby allowing the covalent bonding of the nucleic acids to the surface to proceed. The use of such formulations addnl. minimizes nonspecific binding of the nucleic acids to the surface. Examples of materials to be included in such formulations include cations, xanthenes, hexoses, purines, arginine, lysine, polyarginine, polylysine, and quaternary ammonium salts.

IT 91725-06-3

RL: NUU (Other use, unclassified); USES (Uses)
(cationic materials and methods for covalent bonding nucleic acids to high purity silica surfaces)

RN 91725-06-3 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,8-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:413184 CAPLUS Full-text

DOCUMENT NUMBER: 135:251414

TITLE: Structural predictions of adenosine 2B antagonist affinity using molecular field analysis

AUTHOR(S): Song, Yuqing; Coupar, Ian M.; Iskander, Magdy N.

CORPORATE SOURCE: Department of Medicinal Chemistry, Victorian College of Pharmacy, Monash University, Parkville, 3052, Australia

SOURCE: Quantitative Structure-Activity Relationships (2001), 20(1), 23-30

CODEN: QSARDI; ISSN: 0931-8771

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 08 Jun 2001

AB 3D structural evaluation of the adenosine 2B (A2B) antagonist binding site is the major aim for developing specific selective antagonists. In an attempt to deduce structural properties of the antagonist site, a pharmacophore model was developed using 85 known A2B antagonists. The mol. mechanics optimization methods were used to deduce the likely binding conformations of the antagonists at the binding site. Super-imposition of the antagonists was carried out using fit-atoms. This alignment was used to develop CoMFA models of the A2B antagonist binding site. The models possessed promising predictive ability as indicated by the high cross-validated correlation ($q^2 = 0.752$, $r^2 = 0.982$) and the prediction on the external test set. The analyses showed that

steric and electrostatic interactions contributed to A2B antagonist biol. activity equally. The hydrogen-bond donor nature of the 7-position of xanthine (1 .apprx. 68) and 3-position of alloxazine (83) was essential for the biol. activity. In addition, the presence of more neg. charges on the 1-N position of xanthine and 10-N position of alloxazine increases biol. activity. The bulky aromatic substitutions on the 8-position of xanthine compds. improve activity, while an alkyl substitution on the 1-position of alloxazine might enhance activity. The model generated from this investigation produced important structural requirements, which will be used to optimize the structural complementarity of the antagonists at the A2B binding site.

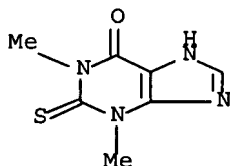
IT 6603-63-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(structural predictions of adenosine 2B antagonist affinity using mol. field anal.)

RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:136945 CAPLUS Full-text

DOCUMENT NUMBER: 134:193441

TITLE: Preparation of hypoxanthines and thiohypoxanthines as phosphodiesterase IV inhibitors

INVENTOR(S): Chasin, Mark; Hofer, Peter; Cavalla, David

PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2001011967 | A1 | 20010222 | WO 2000-US21836 | 20000809 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, | | | |

Serial No.: 10/511,537

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

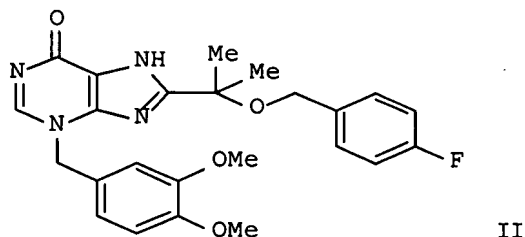
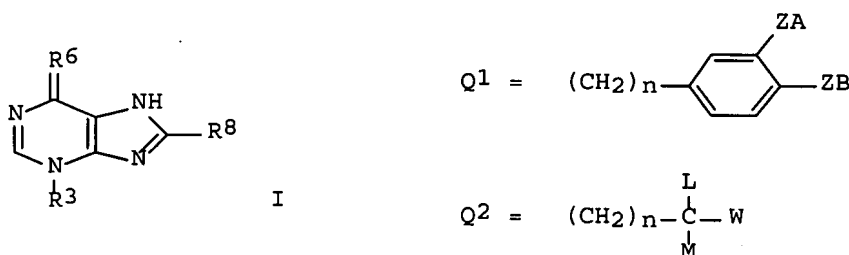
| | | | | |
|------------|----|----------|-----------------|----------|
| CA 2379356 | A1 | 20010222 | CA 2000-2379356 | 20000809 |
| EP 1202628 | A1 | 20020508 | EP 2000-953925 | 20000809 |
| EP 1202628 | B1 | 20041013 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

| | | | | |
|---------------|---|----------|----------------|----------|
| JP 2003506467 | T | 20030218 | JP 2001-516330 | 20000809 |
| AT 279113 | T | 20041015 | AT 2000-953925 | 20000809 |

PRIORITY APPLN. INFO.: US 1999-148623P P 19990812
WO 2000-US21836 W 20000809

OTHER SOURCE(S): MARPAT 134:193441
ED Entered STN: 25 Feb 2001
GI



AB Title compds. (I) [wherein R³ and R⁸ = independently (cyclo)alkyl, alkenyl, alkynyl, Q¹, or Q²; R⁶ = S or O; n = 0-1; Z = a bond, CH₂, NH, O, or S; A and B can form a ring by adding 1-3 CH₂ groups when Z = CH₂, NH, O or S; and A and B are not in a ring when Z = a bond, wherein A and B = independently H, halo, (cyclo)alkyl, (cyclo)alkoxy, OH, or (un)substituted Ph, benzyl, or benzyloxy; L and M = independently H or Me; W = Q¹, OH, (hetero)aryl, heterocyclyl, or (un)substituted benzyloxy] were prepared as selective phosphodiesterase (PDE) IV inhibitors. For example, amidation of 2-(4-fluorobenzyl)-2-methylpropionyl chloride with 5,6-diamino-1-(3,4-dimethoxybenzyl)-2-thiouracil using TEA in THF (20.4%), followed by cyclization with NaOH to form the 2-thioxanthine (79.1%) and treatment with Raney nickel in 1-propanol (67.2%), afforded the hypoxanthine (II). In assays measuring isolated PDE isoenzyme activity, II selectively inhibited PDE IV compared to PDE III and PDE V with IC₅₀ values of 1.079 μM, 69.62 μM, and 35.80 μM, resp. As a result, I are expected to induce the desirable anti-asthmatic effects associated with PDE IV inhibition without causing the undesirable cardiovascular stimulation associated with PDE III inhibition (no data). I are useful in the treatment of asthma, allergies, inflammation, depression, dementia, and other disease states associated with abnormally high physiol. levels of cytokine (no data).

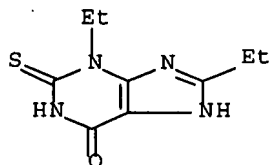
IT 162278-04-8, 3,8-Diethyl-2-thioxanthine

Serial No.: 10/511,537

RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of hypoxanthine and thiohypoxanthine
phosphodiesterase IV inhibitors from thiouracils and acyl halides and
anhydrides)

RN 162278-04-8 CAPLUS

CN 6H-Purin-6-one, 3,8-diethyl-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX
NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:725418 CAPLUS Full-text

DOCUMENT NUMBER: 133:296324

TITLE: Synthesis and phosphodiesterase IV inhibition activity
of purine derivatives

INVENTOR(S): Chasin, Mark; Cavalla, David; Hofer, Peter; Gehrig,
Andre; Wintergest, Peter

PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 21

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2000059449 | A2 | 20001012 | WO 2000-US8525 | 20000331 |
| WO 2000059449 | A3 | 20010104 | | |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| IN 180930 | A1 | 19980404 | IN 1995-CA1508 | 19951123 |
| IN 181538 | A1 | 19980711 | IN 1995-CA1506 | 19951123 |
| CA 2367143 | A1 | 20001012 | CA 2000-2367143 | 20000331 |
| EP 1169321 | A2 | 20020109 | EP 2000-919929 | 20000331 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |
| HU 200200938 | A2 | 20021028 | HU 2002-938 | 20000331 |
| JP 2002541078 | T | 20021203 | JP 2000-609014 | 20000331 |
| BR 2000011182 | A | 20030610 | BR 2000-11182 | 20000331 |
| JP 2001316314 | A | 20011113 | JP 2000-136383 | 20000509 |

PRIORITY APPLN. INFO.:

US 1999-285473

A 19990402

IN 1994-CA514

A1 19940630

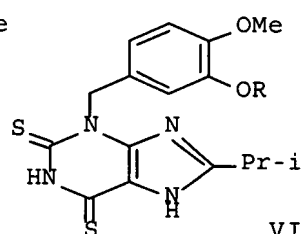
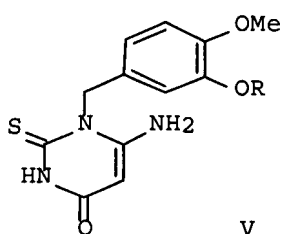
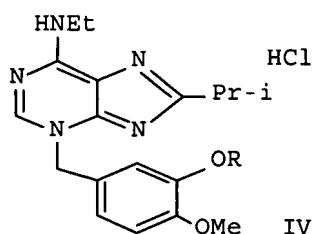
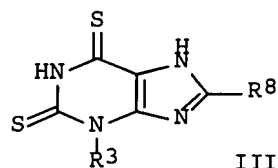
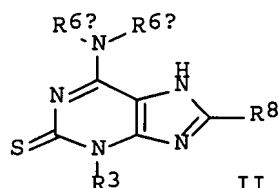
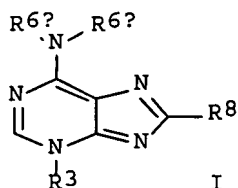
WO 2000-US8525

W 20000331

OTHER SOURCE(S): MARPAT 133:296324

ED Entered STN: 13 Oct 2000

GI



AB The purine (I) (R3, R8, R6a, R6b = H, (un)substituted alkyl, alkenyl, cycloalkyl, aryl, heterocyclyl, heteroaryl etc.), thioisoguanine (II), dithioxanthine (III) derivs., and their pharmaceutically accepted salts were synthesized. Thus, purine (IV; R = (CH2)5) was prepared by etherification of isovanilline with cyclopentanol, oximation, reduction to amine, conversion to isothiocyanate, amination to thiourea followed by heterocyclization with Et cyanoacetate to thiouracil (V). V was nitrosylated, reduced, reacted with isobutyric anhydride to give isobutyrylamine which on treatment with phosphorus pentasulfide gave dithioxanthine (VI). VI, in a pressure reactor gave purine-2-thione which was reduced with Raney-nickel to give IV. The IC50 of IV against phosphodiesterase IV inhibition was 0.32 μ M. I, II and III were effective in effecting PDE IV inhibition in patients in need thereof.

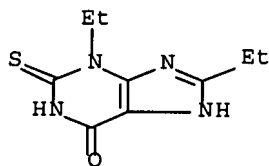
IT 162278-04-8, 3,8-Diethyl-2-thioxanthine

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of purine derivs. as phosphodiesterase IV inhibitors)

RN 162278-04-8 CAPLUS

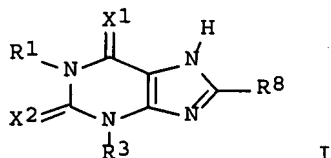
CN 6H-Purin-6-one, 3,8-diethyl-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:113098 CAPLUS Full-text
 DOCUMENT NUMBER: 132:151831
 TITLE: Preparation of thioxanthines as PDE IV inhibitors
 INVENTOR(S): Cavalla, David; Hofer, Peter; Chasin, Mark
 PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg
 SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 476,262,
 abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 21
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| US 6025361 | A | 20000215 | US 1997-860674 | 19970929 |
| IN 180930 | A1 | 19980404 | IN 1995-CA1508 | 19951123 |
| IN 181538 | A1 | 19980711 | IN 1995-CA1506 | 19951123 |
| CA 2206804 | A1 | 19960620 | CA 1995-2206804 | 19951212 |
| CA 2206804 | C | 20020319 | | |
| WO 9618400 | A1 | 19960620 | WO 1995-US16724 | 19951212 |
| W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| IN 1995CA01665 | A | 20050304 | IN 1995-CA1665 | 19951218 |
| US 5977119 | A | 19991102 | US 1997-931849 | 19970915 |
| US 6268373 | B1 | 20010731 | US 1999-361196 | 19990726 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1994-354664 | B2 19941213 |
| | | | US 1995-476262 | B2 19950607 |
| | | | WO 1995-US16724 | W 19951212 |
| | | | IN 1994-CA514 | A1 19940630 |
| | | | US 1997-860674 | A1 19970929 |

OTHER SOURCE(S): MARPAT 132:151831
 ED Entered STN: 17 Feb 2000
 GI



AB Title compds. [I; R1,R3,R8 = alkyl or aryl(alkyl); 1 of X1,X2 = S and the other = O or S] were prepared Thus, 5,6-diamino-1,3-diethyl-2-thiouracil was

Serial No.: 10/511,537

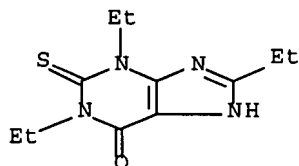
N-acylated by cyclopropanecarbonyl chloride and the cyclized product treated with P4S10 to give I (R1 = R3 = Et, X1 = X2 = S). Data for biol. activity of I were given.

IT 257939-27-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thioxanthines as PDE IV inhibitors)

RN 257939-27-8 CAPLUS

CN 6H-Purin-6-one, 1,3,8-triethyl-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 186 THERE ARE 186 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:412389 CAPLUS Full-text

DOCUMENT NUMBER: 131:179928

TITLE: 1,3-Dialkylxanthine derivatives having high potency as antagonists at human A2b adenosine receptors

AUTHOR(S): Jacobson, Kenneth A.; Ijzerman, Ad P.; Linden, Joel

CORPORATE SOURCE: Molecular Recognition Section, Laboratory of Bioorganic Chemistry, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0810, USA

SOURCE: Drug Development Research (1999), 47(1), 45-53

CODEN: DDREDK; ISSN: 0272-4391

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 05 Jul 1999

AB The structure-activity relationships (SAR) of alkylxanthine derivs. as antagonists at the recombinant human adenosine receptors were explored in order to identify selective antagonists of A2B receptors. The effects of lengthening alkyl substituents from Me to Bu at 1- and 3-positions and addnl. substitution at the 7- and 8-positions were probed. Ki values, determined in competition binding in membranes of HEK-293 cells expressing A2B receptors using 125I-ABOPX (125I-3-(4-amino-3-iodobenzyl)-8-(phenyl-4- oxyacetate)-1-propylxanthine), were approx. 10 to 100 nM for 8-phenylxanthine functionalized congeners. Xanthines containing 8-aryl, 8-alkyl, and 8-cycloalkyl substituents, derivs. of XCC (8-[4-[[[carboxy]methyl]oxy]phenyl]-1,3-dipropylxanthine) and XAC (8-[4-[[[(2-amino-ethyl)amino]carbonyl]methyl]-oxy]phenyl]-1,3-dipropylxanthine), containing various ester and amide groups, including L- and D-amino acid conjugates, were included. Enprofylline was 2-fold more potent than theophylline in A2B receptor binding, and the 2-thio modification was not tolerated. Among the most potent derivs. examined were XCC, its hydrazide and aminoethyl and fluoroethyl amide derivs., XAC, N-

hydroxyethyl-XAC, and the L-citrulline and D-p-aminophenylalanine conjugates of XAC. An N-hydroxysuccinimide ester of XCC (XCC-NHS, MRS 1204) bound to A2B receptors with a K_i of 9.75 nM and was the most selective (at least 20-fold) in this series. In a functional assay of recombinant human A2B receptors, four of these potent xanthines were shown to fully antagonize the effects of NECA-induced stimulation of cAMP accumulation.

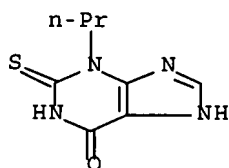
IT 156733-29-8

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(1,3-Dialkylxanthine derivs. having high potency as antagonists at human A2b adenosine receptors)

RN 156733-29-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-propyl-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:441960 CAPLUS Full-text

DOCUMENT NUMBER: 129:109311

TITLE: Preparation of nucleoside uronamides as A3 adenosine receptor agonists

INVENTOR(S): Jacobson, Kenneth A.; Gallo-Rodriguez, Carola; Van Galen, Philip J. M.; Von Lubitz, Dag K. J. E.; Jeong, Heaok Kim

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U.S., 54 pp., Cont.-in-part of U. S. Ser. No. 163,324, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

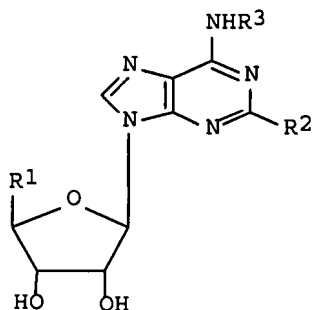
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 5773423 | A | 19980630 | US 1994-274628 | 19940713 |
| US 5688774 | A | 19971118 | US 1995-396111 | 19950228 |
| PRIORITY APPLN. INFO.: | | | US 1993-91109 | B2 19930713 |
| | | | US 1993-163324 | B2 19931206 |
| | | | US 1994-274628 | A2 19940713 |

OTHER SOURCE(S): MARPAT 129:109311

ED Entered STN: 17 Jul 1998

GI



I

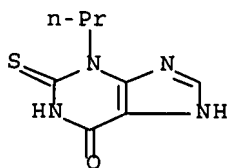
AB The present invention provides N6-benzyladenosine-5'-N-uronamide and related substituted compds. I (R1 = amide; R2 = halo, amino, alkenyl, alkynyl, thio, alkylthio; R3 = S-1-phenylethyl, Bn, phenylethyl), particularly those containing substituents on the benzyl and/or uronamide groups, and modified xanthine ribosides, as well as pharmaceutical compns. containing such compds. The present invention also provides a method of selectively activating an A3 adenosine receptor in a mammal, which method comprises acutely or chronically administering to a mammal in need of selective activation of its A3 adenosine receptor a therapeutically effective amount of a compound which binds with the A3 receptor so as to stimulate an A3 receptor-dependent response. Thus, N6-(3-iodobenzyl)adenosine was prepared tested for its affinity in binding at rat brain A1, A2, A3 adenosine receptors (Ki = 9.5-220.0 nM).

IT 156733-29-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nucleoside uronamides as A3 adenosine receptor agonists)

RN 156733-29-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-propyl-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:331961 CAPLUS Full-text

DOCUMENT NUMBER: 126:305588

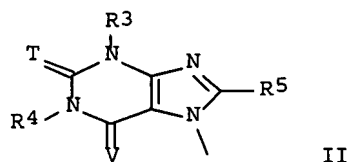
TITLE: Preparation of 4-(dioxopurinylmethyl)phenylacetates and analogs as hypolipemics

INVENTOR(S): Connell, Richard; Goldmann, Siegfried; Mueller, Ulrich; Lohmer, Stefan; Bischoff, Hilmar; Denzer, Dirk; Gruetzmann, Rudi; Wohlfeil, Stefan

PATENT ASSIGNEE(S): Bayer A.-G., Germany

SOURCE: Eur. Pat. Appl., 69 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|------------|
| EP 764647 | A1 | 19970326 | EP 1996-114577 | 19960912 |
| R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| DE 19535504 | A1 | 19970327 | DE 1995-19535504 | 19950925 |
| US 5714494 | A | 19980203 | US 1996-710503 | 19960918 |
| JP 09216884 | A | 19970819 | JP 1996-267691 | 19960919 |
| CA 2186086 | A1 | 19970326 | CA 1996-2186086 | 19960920 |
| PRIORITY APPLN. INFO.: | | | DE 1995-19535504 | A 19950925 |
| OTHER SOURCE(S): | | | MARPAT 126:305588 | |
| ED Entered STN: 24 May 1997 | | | | |
| GI | | | | |



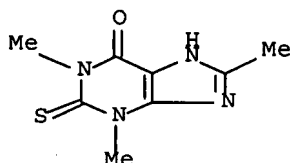
AB RCH₂ZCHR₁C(:L)R₂ [I; R = xanthine moiety, e.g., II; R₁ = H, (cyclo)alkyl, Ph, heterocyclyl, etc.; R₂ = OH, SH, alkoxy, (di)alkylamino, etc.; R₃, R₄ = H, alkyl, aryl, etc.; R₅ = H, halo, alkyl, aryl, etc.; L, T, V = O or S; Z = (un)substituted 1,4-phenylene] were prepared. Thus, 5,6-diamino-1,3-dimethyluracil was cyclocondensed with 4-MeC₆H₄CHO and the product N-alkylated by 4-(BrCH₂)C₆H₄CHR₁CO₂CMe₃ (R₁ = cyclopentyl) (preparation given) to give 4-(RCH₂)C₆H₄CHR₁CO₂CMe₃ (R = II, R₁ = cyclopentyl, R₃ = R₄ = Me, R₅ = C₆H₄Me-4, T = V = O). Data for biol. activity of I were given.

IT 19673-55-3P 189215-37-0P

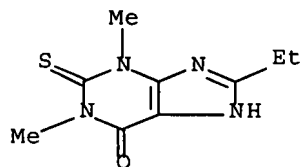
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of 4-(dioxopurinylmethyl)phenylacetates and analogs as hypolipemics)

RN 19673-55-3 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,8-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 189215-37-0 CAPLUS
 CN 6H-Purin-6-one, 8-ethyl-1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI)
 (CA INDEX NAME)



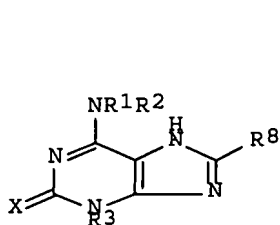
L9 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1995:492020 CAPLUS Full-text
 DOCUMENT NUMBER: 122:239459
 TITLE: Preparation of purines, isoguanines, and
 dithioxanthines as phosphodiesterase-IV inhibitors
 INVENTOR(S): Cavalla, David; Hofer, Peter; Gehrig, Anddre;
 Wintergest, Peter
 PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
 SOURCE: PCT Int. Appl., 75 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 21
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9500516 | A1 | 19950105 | WO 1994-GB1334 | 19940621 |
| W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2165433 | A1 | 19941223 | CA 1994-2165433 | 19940621 |
| CA 2165433 | C | 20020528 | | |
| AU 9469771 | A | 19950117 | AU 1994-69771 | 19940621 |
| AU 683270 | B2 | 19971106 | | |
| EP 705265 | A1 | 19960410 | EP 1994-918456 | 19940621 |
| EP 705265 | B1 | 19990728 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| CN 1125445 | A | 19960626 | CN 1994-192521 | 19940621 |
| CN 1045778 | B | 19991020 | | |
| HU 74176 | A2 | 19961128 | HU 1995-3545 | 19940621 |
| JP 09500376 | T | 19970114 | JP 1995-502570 | 19940621 |
| JP 3350550 | B2 | 20021125 | | |
| EP 916672 | A1 | 19990519 | EP 1999-100735 | 19940621 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| EP 916673 | A1 | 19990519 | EP 1999-100736 | 19940621 |
| EP 916673 | B1 | 20030129 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| AT 182593 | T | 19990815 | AT 1994-918456 | 19940621 |

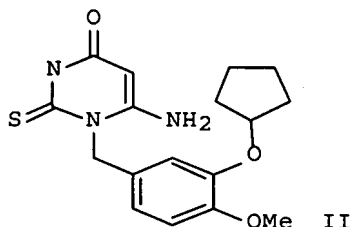
Serial No.: 10/511,537

| | | | | |
|------------------------|----|----------|------------------|-------------|
| ES 2137371 | T3 | 19991216 | ES 1994-918456 | 19940621 |
| NZ 328914 | A | 20000825 | NZ 1994-328914 | 19940621 |
| AT 231863 | T | 20030215 | AT 1999-100736 | 19940621 |
| ZA 9404463 | A | 19950217 | ZA 1994-4463 | 19940622 |
| IN 177888 | A1 | 19970222 | IN 1994-CA514 | 19940630 |
| TW 418208 | B | 20010111 | TW 1994-83107047 | 19940802 |
| IN 180930 | A1 | 19980404 | IN 1995-CA1508 | 19951123 |
| IN 181538 | A1 | 19980711 | IN 1995-CA1506 | 19951123 |
| FI 9506168 | A | 19960201 | FI 1995-6168 | 19951221 |
| NO 9505219 | A | 19960222 | NO 1995-5219 | 19951221 |
| BG 62933 | B1 | 20001130 | BG 1995-100258 | 19951227 |
| US 5939422 | A | 19990817 | US 1996-578580 | 19960408 |
| US 6310205 | B1 | 20011030 | US 1999-237638 | 19990126 |
| US 6294541 | B1 | 20010925 | US 1999-418330 | 19991014 |
| US 6319928 | B1 | 20011120 | US 1999-418331 | 19991014 |
| PRIORITY APPLN. INFO.: | | | GB 1993-12853 | A 19930622 |
| | | | EP 1994-918456 | A3 19940621 |
| | | | NZ 1994-267468 | A1 19940621 |
| | | | WO 1994-GB1334 | W 19940621 |
| | | | IN 1994-CA514 | A1 19940630 |
| | | | US 1996-578580 | A2 19960408 |
| | | | US 1996-659767 | A1 19960606 |
| | | | US 1997-69371P | P 19971212 |
| | | | US 1998-200615 | B2 19981130 |
| | | | US 1998-210556 | A2 19981211 |
| | | | US 1999-285473 | A1 19990402 |

OTHER SOURCE(S): MARPAT 122:239459
 ED Entered STN: 18 Apr 1995
 GI



I



II

AB Title compds. [e.g., I; R₁-R₃, R₈ = H, (cyclo)alkyl, (hetero)aryl, etc.; NR₁R₂ = heterocyclyl] were prepared. Title compds. have bronchial and tracheal relaxation and/or antiinflammatory activity. Thus, isovanillin was converted in 5 steps to 3,4-(HO)(MeO)C₆H₃CH₂NHCSNH₂ which was cyclocondensed with NCCH₂CO₂Et to give thiouracil II. The latter was converted in 3 steps to 6-amino-1-(3-cyclopentyloxy-4-methoxybenzyl)-5-isobutyrylamino-2-thiouracil which was cyclized and the product converted in 4 steps to I.HCl (R₁ = Et, R₂ = H, R₃ = 3-cyclopentyloxy-4-methoxybenzyl, R₈ = CHMe₂) (III). III gave 64% inhibition of ovalbumin-induced bronchoalveolar eosinophil production in guinea pigs at 5mg/kg i.p.

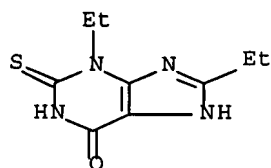
IT 162278-04-8

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of purines, isoguanines, and dithioxanthines as

phosphodiesterase-IV inhibitors)

RN 162278-04-8 CAPLUS

CN 6H-Purin-6-one, 3,8-diethyl-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:500054 CAPLUS Full-text

DOCUMENT NUMBER: 121:100054

TITLE: A binding site model and structure-activity

relationships for the rat A3 adenosine receptor

AUTHOR(S): van Galen, Philip J. M.; van Bergen, Andrew H.;
Gallo-Rodriguez, Carola; Melman, Neli; Olah, Mark E.;
Ijzerman, Ad P.; Stiles, Gary L.; Jacobson, Kenneth A.CORPORATE SOURCE: Lab. Bioorganic Chem., Natl. Inst. Diabetes, Digestive
and Kidney Diseases, Bethesda, MD, 20892, USA

SOURCE: Molecular Pharmacology (1994), 45(6), 1101-11

CODEN: MOPMA3; ISSN: 0026-895X

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 03 Sep 1994

AB A novel adenosine receptor, the A3 receptor, has recently been cloned. The authors have systematically investigated the hitherto largely unexplored structure-activity relationships (SARs) for binding at A3 receptors, using 125I-N6-2-(4-aminophenyl)ethyladenosine as a radioligand and membranes from Chinese hamster ovary cells stably transfected with the rat A3-cDNA. As is the case for A1 and A2a receptors, substitutions at the N6 and 5' positions of adenosine, the prototypic agonist ligand, may yield fairly potent compds. However, the highest affinity and A3 selectivity is found for N6,5'-disubstituted compds., in contrast to A2 and A2a receptors. Thus, N6-benzyladenosine-5'-N-ethylcarboxamide is highly potent (K_i , 6.8 nM) and moderately selective (13- and 14-fold vs. A1 and A2a). The N6 region of the A3 receptor also appears to tolerate hydrophilic substitutions, in sharp contrast to the other subtypes. Potencies of N6,5'-disubstituted compds. in inhibition of adenylate cyclase via A3 receptors parallel their high affinity in the binding assay. None of the typical xanthine or nonxanthine (A1/A2) antagonists tested show any appreciable affinity for rat A3 receptors. 1,3-Dialkylxanthines did not antagonize the A3 agonist-induced inhibition of adenylate cyclase. A His residue in helix 6 that is absent in A3 receptors but present in A1/A2 receptors may be causal in this respect. In a mol. model for the rat A3 receptor, this mutation, together with an increased bulkiness of residues surrounding the ligand, make antagonist binding unfavorable when compared with a previously developed A1 receptor model. Second, this A3 receptor model predicted similarities with A1 and A2 receptors in the binding requirements for the ribose moiety and that xanthine-7-ribosides would bind to rat A3 receptors. This hypothesis was supported exptl. by the moderate affinity (K_i , 6 μ M) of 7-riboside of 1,3-dibutylxanthine, which appears to be a partial agonist at rat A3 receptors. The model presented here which is

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consistent with the detailed SAR found in this study, may serve to suggest future chemical modification, site-directed mutagenesis, and SAR studies to further define essential characteristics of the ligand-receptor interaction and to develop even more potent and selective A3 receptor ligands.

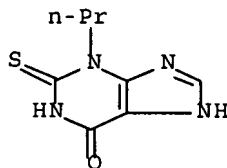
IT 156733-29-8

RL: BIOL (Biological study)

(adenosine A1 and A2a and A3 receptors affinity for, mol. structure in relation to)

RN 156733-29-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-propyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:644995 CAPLUS Full-text

DOCUMENT NUMBER: 117:244995

TITLE: Approach to an adenosine pharmacophore by molecular modeling

AUTHOR(S): Neuwels, M.

CORPORATE SOURCE: UCB Sect. Pharm., Chemin Foriest, Braine-l-Alleud, B-1420, Belg.

SOURCE: Journal de Pharmacie de Belgique (1992), 47(4), 351-63
CODEN: JPBEAJ; ISSN: 0047-2166

DOCUMENT TYPE: Journal

LANGUAGE: French

ED Entered STN: 26 Dec 1992

AB The selective development of adenosine A1 antagonists was carried out in 2 steps. First an A1 pharmacophore common to various known chemical families was determined in order to permit the design of new chemical skeletons; then a predictive modeling of affinities was carried out to select new potential ligands. The mol. modeling was done on 6 different chemical families (triazoloquinoxalines, adenines, xanthines, pyrazolopyrimidinones, triazoloquinazolines, and imidazoquinolines), and a search for a common superimposition was carried out. Starting from the different superpositions obtained, a ComFA study (QSAR-3D) allowed the building of predictive models for A1 receptor affinity. The theor. preferred superposition proved to be the best, as it was able to correctly predict the activities of new ligands.

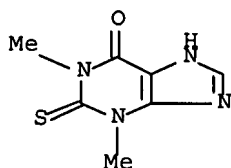
IT 6603-63-0

RL: BIOL (Biological study)

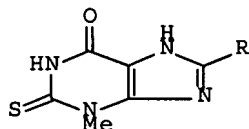
(in mol. modeling of adenosine receptor pharmacophore)

RN 6603-63-0 CAPLUS

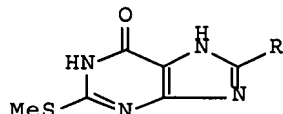
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1992:426495 CAPLUS Full-text
 DOCUMENT NUMBER: 117:26495
 TITLE: Facile and general synthesis of 8-substituted
 2-(methylthio)purin-6-ones
 AUTHOR(S): Nagamatsu, Tomohisa; Yamasaki, Hiroo
 CORPORATE SOURCE: Fac. Pharm. Sci., Okayama Univ., Tsushima, 700, Japan
 SOURCE: Heterocycles (1992), 33(2), 775-90
 CODEN: HTCYAM; ISSN: 0385-5414
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 117:26495
 ED Entered STN: 26 Jul 1992
 GI



I

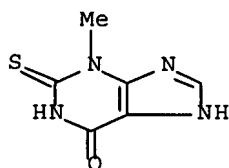


II

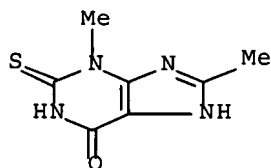
AB 3-Methyl-6-oxo-2-thioxo-1,2,3,6-tetrahydropurines [I; R = H, alkyl, (un)substituted Ph] were synthesized by oxidative cyclization of 5,6-diamino-1-methyl-2-thiouracil-RCHO reaction products or 6-amino-5-(benzylideneamino)-1-methyl-2-thiouracils in the presence of di-Et azodicarboxylate (DEAD). In addition, the oxidative cyclization of 4-amino-5-(benzylideneamino)-3-methyl-2-(methylthio)pyrimidin-6(3H)-ones in the presence of DEAD gave 8-aryl-3-methyl-2-(methylthio)-6-oxo-3,6-dihydropurines, which were identical with the compds. prepared by methylation of I. 2-(Methylthio)-6-oxo-1,6-dihydropurines [II; R = H, alkyl, (un)substituted Ph] were synthesized from 4,5-diamino-2-(methylthio)pyrimidin-6(1H)-one or 4-amino-5-(benzylideneamino)-2-(methylthio)pyrimidin-6(1H)-ones in a similar manner as above.

IT 28139-02-8P 91725-06-3P 103289-69-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and methylation of)

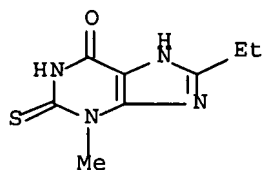
RN 28139-02-8 CAPLUS
 CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



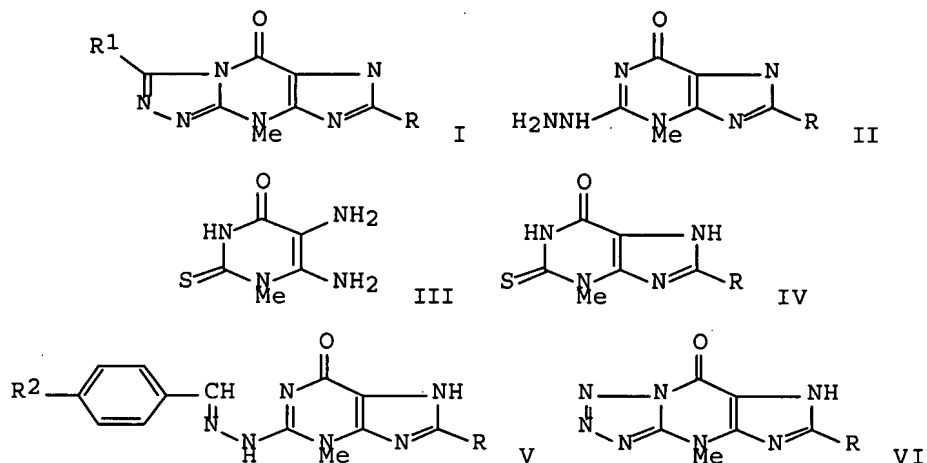
RN 91725-06-3 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,8-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 103289-69-6 CAPLUS
CN 6H-Purin-6-one, 8-ethyl-1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:478896 CAPLUS Full-text
DOCUMENT NUMBER: 105:78896
TITLE: Syntheses of 4-methyl-s-triazolo[4,3-a]purin-9(4H)-ones and tetrazolo[1,5-a]purin-9(4H)-ones as aza analogs of "Y" bases
AUTHOR(S): Nagamatsu, Tomohisa; Ukai, Masayoshi; Yoneda, Fumio; Brown, Desmond J.
CORPORATE SOURCE: Fac. Pharm. Sci., Kumamoto Univ., Kumamoto, 862, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1985), 33(8), 3113-21
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:78896
ED Entered STN: 06 Sep 1986
GI



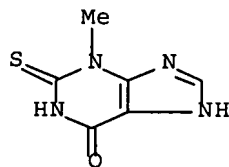
AB 4-Methyl-s-triazolo[4,3-a]purin-9(4H)-ones I (R = H, Me, Et, Ph; R1 = H, Me, Et) were prepared by the cyclocondensation of purin-6(3H)-ones II (R = same) with the appropriate R1C(OEt)3. II were prepared by cyclizing pyrimidine III with RC(OEt)3 and treating the resulting thioxanthines IV with NH2NH2. I [R = Me, Et, Ph; R1 = p-R2C6H4 (R2 = H, Me, Cl, OMe)] were prepared by the condensation of the appropriate II with p-R2C6H4CHO, followed by the oxidative cyclization of the resulting arylidenehydrazine derivs. V. I (R = Me, Et; R1 = SH, SMe, SEt, SCH2CONH2) were also prepared Tetrazolo[1,5-a]purin-9(4H)-ones VI (R = H, Me, Et, Ph) were prepared by treating the corresponding II with NaNO2/HCl.

IT 28139-02-8P 91725-06-3P 103289-69-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with hydrazine)

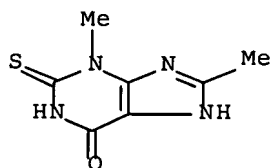
RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)

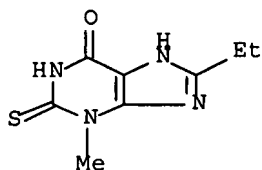


RN 91725-06-3 CAPLUS

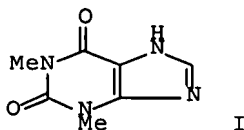
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,8-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 103289-69-6 CAPLUS
 CN 6H-Purin-6-one, 8-ethyl-1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1983:119142 CAPLUS Full-text
 DOCUMENT NUMBER: 98:119142
 TITLE: Alkylxanthines as adenosine receptor antagonists and membrane phosphodiesterase inhibitors in central nervous tissue: evaluation of structure-activity relationships
 AUTHOR(S): Wu, P. H.; Phillis, J. W.; Nye, M. J.
 CORPORATE SOURCE: Coll. Med., Univ. Saskatchewan, Saskatoon, SK, Can.
 SOURCE: Life Sciences (1982), 31(25), 2857-67
 CODEN: LIFSAK; ISSN: 0024-3205
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 12 May 1984
 GI



AB A series of alkylxanthines were examined as antagonists of the adenosine [58-61-7] A1-receptor in rat brain synaptosomal membranes and as inhibitors of membrane phosphodiesterase [9025-82-5]. Structure-activity relations showed that the addition of certain substituting groups at position 8 of the theophylline mol. produced mol. structures which generally favored adenosine receptor antagonism. This is evident from the potency order of 8-substituted

theophyllines as adenosine receptor antagonists: 8-(p-bromophenyl)theophylline [63325-99-5], 8-(p-methylphenyl)theophylline [57196-70-0], 8-phenyltheophylline [961-45-5] and 8-(p-chlorophenyl)theophylline [29064-02-6], 8-(methoxyphenyl)theophylline [84942-90-5] > 8-(dimethylaminophenyl)theophylline [54013-59-1] > 8-benzyltheophylline [2879-15-4] > theophylline (I) [58-55-9]. The order of potency for inhibition of brain membrane phosphodiesterase was: 1,3-dimethyl-2,6-dithioxopurine [6501-94-6] > methylxanthines > 8-substituted theophyllines. 8-Substituted theophyllines may be selective in their activity as adenosine receptor antagonists, whereas an increase in lipid solubility by substitution at the 1, 2, 3, and 6 positions of the purine ring may result in an increase in phosphodiesterase inhibition.

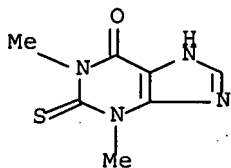
IT 6603-63-0 24049-32-9

RL: BIOL (Biological study)

(adenosine receptor and phosphodiesterase of synaptosome membrane response to, alkylxanthines effect on)

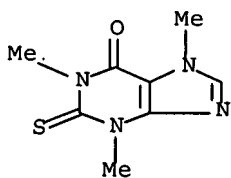
RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 24049-32-9 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:435269 CAPLUS Full-text

DOCUMENT NUMBER: 95:35269

TITLE: Adenosine antagonism by purines, pteridines, and benzopteridines in human fibroblasts

AUTHOR(S): Bruns, Robert F.

CORPORATE SOURCE: Dep. Neurosci., Univ. California, La Jolla, CA, 92093, USA

SOURCE: Biochemical Pharmacology (1981), 30(4), 325-33

CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

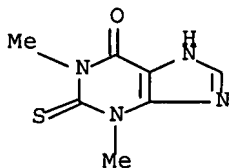
ED Entered STN: 12 May 1984

AB Testing of >100 purine bases and structurally related heterocycles as adenosine (I) [58-61-7] antagonists in VA13 fibroblasts (determined by cAMP increase) yielded 3 families of I antagonists: xanthines, benzo[g]pteridines, and 9-substituted adenines. For the xanthines, the optimal group at the 1-position was Bu (5-fold improvement vs. Me), at the 7-position was 2-chloroethyl (5-fold improvement vs. H), and at the 8-position was p-bromophenyl (100-fold improvement vs. H). The receptors apparently had butyl- and phenyl-sized pockets at the 1- and 8-positions, resp., since compds. with larger groups had greatly reduced activity.

IT 6603-63-0
RL: BIOL (Biological study)
(adenosine receptor of fibroblast antagonism by)

RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:37755 CAPLUS Full-text

DOCUMENT NUMBER: 88:37755

TITLE: Reaction of iodides of 2-methylthio-N,N'-dimethyl-and -N,N',N''-trimethylhypoxanthiniums and their 8-aza analogs during heating and alkylation

AUTHOR(S): Muravich-Aleksandr, Kh. L.; Kolesova, M. B.; Mezhonova, S. S.; Smirnova, N. V.

CORPORATE SOURCE: USSR

SOURCE: Zhurnal Organicheskoi Khimii (1977), 13(8), 1780-7
CODEN: ZORKAE; ISSN: 0514-7492

DOCUMENT TYPE: Journal

LANGUAGE: Russian

ED Entered STN: 12 May 1984

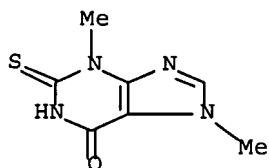
GI For diagram(s), see printed CA Issue.

AB Thermal transformation of hypoxanthinium iodide I 75 min at 195° gave 13% II (R = Me), 5% III (R = Me) 41% thione IV (R = Me), and 41% IV (R = H). Analogously II (R = Me) 75 min at 225° gave 54% starting material, 19% III (R = Me) and 27% IV (R = Me); II (R = H) under identical conditions gave 24% II (R = Me), 36% starting material, 7% III (R = H), 11% III (R = Me), 17% IV (R = H), and 5% IV (R = Me).

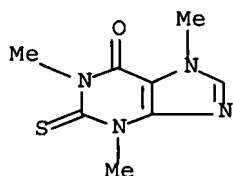
IT 19373-97-8P 24049-32-9P
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in thermal transformations of hypoxanthinium derivs.)

RN 19373-97-8 CAPLUS

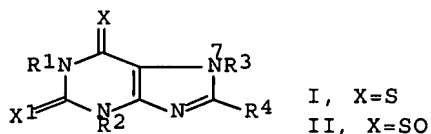
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,7-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 24049-32-9 CAPLUS
 CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1977:453218 CAPLUS Full-text
 DOCUMENT NUMBER: 87:53218
 TITLE: 6-Sulfinyl derivatives of xanthines
 AUTHOR(S): Bergmann, Felix; Frank, Arie; Weiler-Feilchenfeld, Hanna; Tamir, Ilana
 CORPORATE SOURCE: Hadassah Med. Sch., Hebrew Univ., Jerusalem, Israel
 SOURCE: Journal of Organic Chemistry (1977), 42(14), 2470-3
 CODEN: JOCEAH; ISSN: 0022-3263
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 12 May 1984
 GI



AB 6-Thiopurines I ($R_1 = R_4 = H$, $R_2 = R_3 = Me$, $X_1 = O$; $R_1 = R_2 = Me$, $R_3 = R_4 = H$, $X_1 = O, S$; $R_1 = R_2 = Me$, $R_3 = H$, $R_4 = Ph$, $X_1 = O, S$) are oxidized by H_2O_2 or by $BzOOH$ to 6-sulfinylpurines II. Only theophylline derivs. of these unstable II were obtained in pure form. The isomers formed have the 6-sulfinyl group directed toward the 7-NH due to stabilization by an intramol. H bridge. Their structure has been derived from dipole moments and from the chemical shift of

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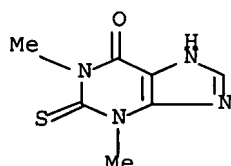
the 1-Me substituent. The 2-thiocarbonyl group in 2-thiotheophyllines is not attacked by the oxidants used, which convert 6-selenoxanthines to the corresponding xanthines.

IT 6603-63-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of)

RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1974:82889 CAPLUS Full-text

DOCUMENT NUMBER: 80:82889

TITLE: Tautomerism, ionization, and methylation of
2-(methylthio)- and 2,8-bis(methylthio)hypoxanthines
AUTHOR(S): Reichman, Uri; Bergmann, Felix; Lichtenberg, Dov
CORPORATE SOURCE: Dep. Pharmacol., Heb. Univ., Jerusalem, Israel
SOURCE: Journal of the Chemical Society, Perkin Transactions
1: Organic and Bio-Organic Chemistry (1972-1999)
(1973), (22), 2647-55
CODEN: JCPRB4; ISSN: 0300-922X

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 May 1984

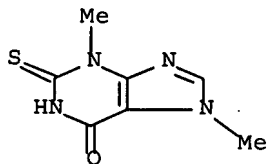
AB Anion formation in the title compds. occurred first at N-1 and then at N-7(9). Protonation involved the imidazole ring except for 3-Me derivs. which were protonated at N-1. Methylation of 3-Me derivs. of the title compds. occurred preferentially at N-7. The formation of cations of partial structure [RNC(SMe)NMe]⁺ was followed by S-demethylation.

IT 19373-97-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 19373-97-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,7-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1971:434696 CAPLUS Full-text

DOCUMENT NUMBER: 75:34696

TITLE: Nuclear magnetic resonance spectra of xanthenes and thioxanthenes

AUTHOR(S): Bergmann, F.; Lichtenberg, D.; Neiman, Z.

CORPORATE SOURCE: Hadassah Med. Sch., Heb. Univ., Jerusalem, Israel

SOURCE: Journal of the Chemical Society [Section] C: Organic (1971), (10), 1939-41

CODEN: JSOOAX; ISSN: 0022-4952

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 May 1984

AB The NMR signal of the 8-H in xanthenes is shifted downfield more strongly by introduction of a 2- than of a 6-thioxo group. The signals of N-Me groups are also shifted to lower field, but the effect depends strictly on the distance between the Me and the thioxo. In 2-thioxanthenes, the displacement decreases in the order 1-Me = 3-Me > 7-Me, and in 6-thioxanthenes the sequence is 1-Me > 7-Me > 3-Me > 9-Me.

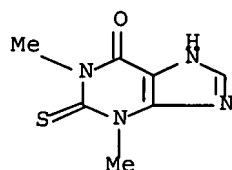
IT 6603-63-0 24049-32-9 28139-02-8

RL: PRP (Properties)

(nuclear magnetic resonance of)

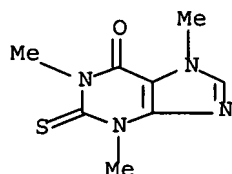
RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



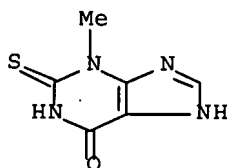
RN 24049-32-9 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)

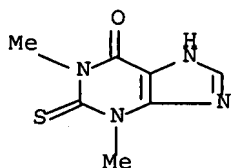


RN 28139-02-8 CAPLUS

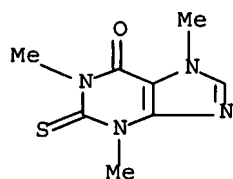
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



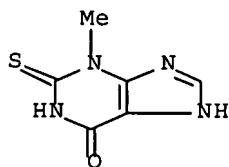
L9 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1970:403341 CAPLUS Full-text
 DOCUMENT NUMBER: 73:3341
 TITLE: Dipole moments and electronic structure of some
 xanthine and thioxanthine derivatives
 AUTHOR(S): Weiler-Feilchenfeld, Hannah; Neiman, Zohar
 CORPORATE SOURCE: Dep. Org. Chem., Hebrew Univ., Jerusalem, Israel
 SOURCE: Journal of the Chemical Society [Section] B: Physical
 Organic (1970), 4, 596-8
 CODEN: JCSPAC; ISSN: 0045-6470
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 12 May 1984
 AB The dipole moments and uv absorption spectra of caffeine, theophylline, and
 their 2-thio-, 6-thio- and 2,6-dithio derivs. were measured. From the
 differences between the moments of these compounds it can be deduced that the
 C:S group moment is higher by 1.1 D than that of C:O; the direction of the
 moment of caffeine forms an angle of 96° counterclockwise with the C(4) →
 C(5) axis, in good agreement with theoretical predictions.
 IT 6603-63-0 24049-32-9
 RL: PRP (Properties)
 (dipole moment of)
 RN 6603-63-0 CAPLUS
 CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX
 NAME)



RN 24049-32-9 CAPLUS
 CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA
 INDEX NAME)



L9 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1970:126337 CAPLUS Full-text
 DOCUMENT NUMBER: 72:126337
 TITLE: Mass spectrometric investigations of heterocyclic compounds. V. Fragmentation of some purines
 AUTHOR(S): Heiss, Juergen; Zeller, Klaus P.; Voelter, Wolfgang
 CORPORATE SOURCE: Chem. Inst., Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.
 SOURCE: Organic Mass Spectrometry (1970), 3(2), 181-90
 CODEN: ORMSBG; ISSN: 0030-493X
 DOCUMENT TYPE: Journal
 LANGUAGE: German
 ED Entered STN: 12 May 1984
 AB The mass spectra of 9 purines are discussed. The xanthine purines eliminate HNCO and CO consecutively, whereas 3-methylhypoxanthine loses HCN and CO. In the case of 3-methylxanthine, an ion is formed whose stabilization by rearrangement is discussed. The fragmentation patterns of 3-methyl-2-thioxanthine and 3-methylthiohypoxanthine are different from those of the corresponding O analogs. 6-(Methylthio)purine and 6-methoxypurine eliminate HCS· or HCO·, resp. For the latter reaction a mechanism is suggested.
 IT 28139-02-8
 RL: PRP (Properties)
 (mass spectrum of)
 RN 28139-02-8 CAPLUS
 CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1969:512889 CAPLUS Full-text
 DOCUMENT NUMBER: 71:112889
 TITLE: Syntheses in the purine series. XX. Effect of chloride compounds of phosphorus on 8-methyltheobromine
 AUTHOR(S): Gutorov, L. A.; Golovchinskaya, E. S.
 CORPORATE SOURCE: Vses. Nauch.-Issled. Khim.-Farm. Inst. im. Ordzhonikidze, Moscow, USSR

SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1969), 3(7), 4-10
 CODEN: KHFZAN; ISSN: 0023-1134

DOCUMENT TYPE: Journal

LANGUAGE: Russian

ED Entered STN: 12 May 1984

GI For diagram(s), see printed CA Issue.

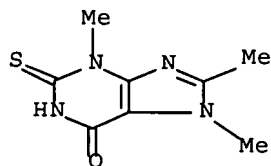
AB To 3 g. 8-methyltheobromine (I) in 15 ml. POCl₃ was added 6.45 g. PCl₅ and the mixture boiled 4 hrs. to give 0.8 g. 2,6-dichloro-7,8-dimethylpurine (II), m. 149-50° (H₂O). From I were prepared III (X = Cl) (IIIa) and IV (X = Cl) (IVa), which were converted to other derivs. Thus, 60 g. I was boiled 4-6 hrs. in 400 ml. POCl₃, the solution concentrated and added to 900 g. ice and 700-800 g. NaHCO₃, the mixture filtered, and the residue extracted with CHCl₃ to give 28-9 g. IIIa, m. 235-8° (PhMe). The aqueous filtrate was extracted with CHCl₃ and the extract concentrated to 50 ml. to give .apprx.68% IVa, m. 241-2° (PhMe). III (X = OEt), m. 176° (C₆H₆), was obtained in 43% yield when NaOEt solution (from 0.2 g. Na and 10 ml. EtOH) was added dropwise to 1.8 g. IIIa in 5 ml. EtOH. Similarly, IVa gave 43% IV (X = OEt), m. 270-1° (alc.). IIIa (0.35 g.) was boiled 1.5 hrs. in 10 ml. 25% NH₄OH and the product filtered off, dissolved in N HCl and precipitated with 2N NaOH to give 63% III (X = NH₂), m. 338-40°. IV (X = NH₂), m. 311-12°, 82.6%, was obtained similarly. IIIa (1.7 g.) in 10 ml. 30% NHMe₂ gave 79% III (X = NMe₂) 1.4 g., m. 168-9° (C₆H₆). Similarly obtained was 72% IV (X = NMe₂), m. 196-200° (C₆H₆). III (X = SH) (IIIb), m. 277-9° (alc.), 95%, and IV (X = SH) (IVb), m. 314-16° (HCONMe₂), 99%, were similarly obtained from alc. thiourea. IIIb and IVb were converted, resp., to III (X = SMe), m. 223-5° (C₆H₆), 74%, and IV (X = SMe), m. 252-3° (alc.), .apprx.100%, by shaking their solns. in N NaOH with MeI and extracting with CHCl₃. IIIa (10 g.) and Na malonate (from 2.8 g. Na and 28 ml. malonic ester), was mixed 1 hr., H₂O added to dissolve the precipitate and the aqueous layer treated with 40% H₂SO₄ to pH 5 to give III [X = CH(CO₂Et)₂] (IIIc), m. 160-1° (alc.), (yield 11.7 g.). Similarly obtained was 95% III [X = CH(CO₂Et)₂] (IVc), m. 211-12°, IIIc (3 g.) was boiled 30 min. with 15 ml. 18% HCl to give 93% 1.6 g. III (X = Me), m. 213-14° (Me₂CO). Similarly, IVc gave 95% IV (X = Me), m. 259-61°. To 1 g. IIIc in 15 ml. CHCl₃ was added 0.25 ml. SO₂Cl₂ in 1 ml. CHCl₃ and the mixture kept 12 hrs. to give 1 g. III [X = CCl(CO₂Et)₂], m. 139-40° (CCl₄). Similarly, IVc gave 95% IV [X = CCl(CO₂Et)₂], m. 176-7°. To prepare III (X = NHMe), m. 359-60°, 1 g. IIIa was dissolved in 3 ml. 30% NH₂Me. IIIa (4.4 g.) was heated at 40-50° with 1.35 g. KCN or 1.9 g. CuCN in 45 ml. HCONMe₂ to give 3.1 g. III (X = CN), m. 194-5° (PhMe).

IT 24168-14-7P

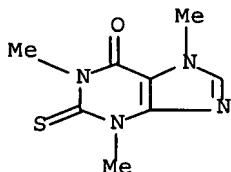
RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 24168-14-7 CAPLUS

CN Xanthine, 3,7,8-trimethyl-2-thio- (8CI) (CA INDEX NAME)



DOCUMENT NUMBER: 71:91430
 TITLE: Chemistry of nucleophilic carbenes. XVI.
 2-Thiocaffeine and 5-oxo-7-methylimino-1,4-dimethyl-
 1,4,5,7-tetrahydroimidazo[4,5-d][1,3]thiazine
 AUTHOR(S): Walentowski, Ruediger; Wanzlick, Hans W.
 CORPORATE SOURCE: Tech. Univ. Berlin, Berlin, Fed. Rep. Ger.
 SOURCE: Chemische Berichte (1969), 102(9), 3000-5
 CODEN: CHBEAM; ISSN: 0009-2940
 DOCUMENT TYPE: Journal
 LANGUAGE: German
 ED Entered STN: 12 May 1984
 GI For diagram(s), see printed CA Issue.
 AB 1,3,7-Trimethylhypoxanthinium nitrate, prepared from 1-methyl-4-methylamino-
 5-(N-methylcarbamoyl)imidazole, was treated with S to give 2-thiocaffeine [5-
 thioxo-7-oxo-1,4,6-trimethyl-4,5,6,7-tetrahydroimidazo-[4,5- d]pyrimidine]
 (I). The "2-thiocaffeine" described by H. Biltz and H. Rakett (1928), was
 found to be 5-oxo-7-methylimino-1,4-dimethyl-4,5- dihydro-7H-imidazo[4,5-
 d]thiazine (II).
 IT 24049-32-9P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 24049-32-9 CAPLUS
 CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA
 INDEX NAME)



L9 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1968:496632 CAPLUS Full-text
 DOCUMENT NUMBER: 69:96632
 TITLE: Reactions of 4,5-diaminouracils with β -oxoesters
 AUTHOR(S): Stahl, P. H.; Merz, K. W.
 CORPORATE SOURCE: Univ. Freiburg/Br., Freiburg/Br., Fed. Rep. Ger.
 SOURCE: Pharmazie (1967), 22(11), 630-4
 CODEN: PHARAT; ISSN: 0031-7144
 DOCUMENT TYPE: Journal
 LANGUAGE: German
 ED Entered STN: 12 May 1984
 GI For diagram(s), see printed CA Issue.
 AB 5,6-Diamino-1,3-dimethyluracil (I) refluxed with an equimol. amount of
 AcCH₂CO₂Et gave 80% II (X = Y = O, R = Me), decompose 216-19°; 2,4-
 dinitrophenylhydrazone m. 255-8°. Following II were prepared (X, Y, R, m.p.,
 m.p. after resolidification, and m.p. of 2,4- dinitrophenylhydrazone given):
 O, O, Ph, 250-2°, 310-40°, 268-70°; O, O, 4-O₂NC₆H₄, 259-63°, 360°, -; O, O,
 pyridin-3-yl, 260-3°, 245°, 261-2°; O, O, α -furyl, 224-32°, -, -; O, S, Me,
 225-8°, -, -; S, S, Me, 212°, -, -; O, S, Ph, 223-9°, -, -; S, O, pyridin-3-
 yl, 257-63°, -, -; O, S, pyridin-3-yl, 244-53°, -, -; S, O, 4-O₂NC₆H₄, 230-5°,
 290-300°, -, -; O, S, 4-O₂NC₆H₄, 240-2°, -, -; S, S, 4-O₂NC₆H₄, 225°, -, -. 1,3-
 Dimethyl-4,5-diamino-2-thiouracil (3.7 g.) and 2.6 g. AcCH₂CO₂Et refluxed in

Serial No.: 10/511,537

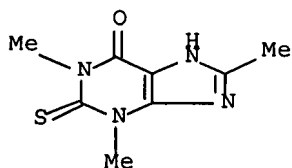
xylene 5 hrs. gave 86% 2,3,6,7,8,9-hexahydro-4,6,8-trimethyl-7-thio-2,9-dioxo-1H-pyrimido[4,5b] - 1,5-diazepine, m. 240-90°, which was converted into 1,3-dimethyl-4-amino-5-(acetoacetyl-amino)-2-thiouracil; 2,4-dinitrophenylhydrazone m. 245-7°. Also prepared was 1,3-dimethyl-4-amino-5-(1-ethoxycarbonyl-2-propylideneamino)-2-thiouracil, m. 210-22° (after resolidification m. 320-30°), which, heated to 250° and treated with NaOH gave 44% 8-methyl-2-thiotheophylline, m. 340-3°. I (2.55 g.) refluxed with 10 g. AcCH₂CO₂Et in 100 ml. PhNO₂ gave 45.4% 8-methyltheophylline, m. 330°; picrate m. 282-305°.

IT 19673-55-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 19673-55-3 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,8-trimethyl-2-thioxo- (9CI) (CA
INDEX NAME)



L9 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1968:427585 CAPLUS Full-text

DOCUMENT NUMBER: 69:27585

TITLE: Preparing theobromine derivatives substituted in the 2 position

INVENTOR(S): Golovchinskaya, E. S.; Nikolaeva, L. A.; Ovcharova, I. M.

PATENT ASSIGNEE(S): Ordzhonikidze, S., All-Union Scientific-Research Chemical-Pharmaceutical Institute

SOURCE: U.S.S.R. From: Izobret., Prom. Obraztsy, Tovarnye Znaki 1967 44(19), 36.

CODEN: URXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Russian

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| SU 202153 | | 19670914 | SU | 19660727 |

ED Entered STN: 12 May 1984

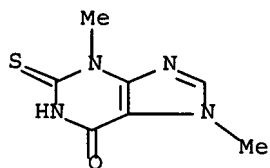
AB The title compds. are prepared from the reaction of theobromine with POCl₃ with boiling; the excess POCl₃ is distilled from the reaction mass, the residue treated with a mixture of ice and NaHCO₃ at a pH of 6-7 and the resulting 2-chlorotheobromine treated with nucleophilic reagents with boiling, e.g., with a 25% aqueous solution of NH₃, thiourea, an alc. solution of Na alcoholate, or Na malonate, in PhMe.

IT 19373-97-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 19373-97-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,7-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1966:420841 CAPLUS Full-text

DOCUMENT NUMBER: 65:20841

ORIGINAL REFERENCE NO.: 65:3877f-h,3878a-c

TITLE: Purine derivatives. III. Sulfur-containing theophyllines. I

AUTHOR(S): Merz, K. W.; Stahl, P. H.

CORPORATE SOURCE: Univ. Freiburg/Br., Germany

SOURCE: Beitr. Biochem. Physiol. Naturstoffen, Festschr. (1965) 285-98

DOCUMENT TYPE: Journal

LANGUAGE: German

ED Entered STN: 22 Apr 2001

GI For diagram(s), see printed CA Issue.

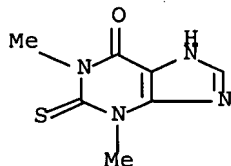
AB cf. CA 63, 4296b. It is easy to prepare 6-thiotheophylline (I) by heating theophylline with P4S10 in a pyridine base b. 140-60° but 2,6-dithiotheophylline (II) can only be prepared (in very small quantities) from theophylline by melting it together with P4S10. 2-Thiotheophylline (III) was prepared first. Ethyl cyanoacetate, N,N'-dimethylthiourea, and NaOMe was refluxed 15 hrs. in a mol. ratio of 1.5:1:1.5 to give 34.5% 1,3-dimethyl-4-amino-2-thiouracil (IV), m. 289-90°. IV suspended in H2O and AcOH, or in HCONH2, was cooled in ice and NaNO2 added dropwise to give blue-green 1,3-dimethyl-4-amino-5-nitroso-2-thiouracil (V), m. 218-20°. V was reduced with Na dithionate at 100°, when 2-5 g. IV was used. When 10-30 g. IV was used, Na dithionate was used as starter, but the reduction itself was effected by formic acid. In both cases, 1,3-dimethyl-4,5-diamino-2-thiouracil (VI), m. 240-3°, was formed, and when HCONH2 was still present, 1,3-dimethyl-4-amino-5-formylamino-2-thiouracil (VII), m. 304-5°, was formed immediately. By heating VII for 0.5 hr., III, m. 344-8°, was formed, from which II, m. 267-9°, was prepared with P4S10 in pyridine with 1% H2O. It was not possible to prepare the nitroso compound from the orange 1,3dimethyl-4-amino- 2,6-dithiouracil (VIII), m. 273-5° (prepared from IV with P4S10), or from 1,3-dimethyl-4-amino-6-thiouracil (IX), m. 283-6° because of the lower electronegativity of the S, compound with the original O. By boiling 1,3-dimethyl-4,5-diaminouracil (X) or VI 12 hrs. with P4S10 in pyridine, 1,3-dimethyl-4,5-diamino-6-thiouracil (XI), and 1,3-dimethyl-4,5-diamino-2,6-dithiouracil (XII) were prepared, resp. With formamide the ring was closed and I, m. 311°, and II, were formed. From VI in stoichiometric ratio with HNO2 4,5,6,7-tetrahydro-4,6-dimethyl- 5-thio-7-oxo-v-triazolo[4,5-d]pyrimidine (XIII), m. 229°, was obtained; this was not possible with XI and XII. The S in III and I was substituted by 2H, by boiling the compound with Raney Ni in a dilute NH3 solution, to give 1,2,3,6-tetrahydro-1,3-dimethyl-6-oxopurine (XIV), and 1,2,3,6-tetrahydro-1,3-dimethyl-2-oxopurine (XV), resp., but neither of the S atoms could be substituted in the same way in II.

Identification was by thin-layer chromatography on silica gel with 80:12:5 C₆H₆-EtOHAcOH. In the uv spectra of the compds. a bathochromic shift of the absorption bands with regard to theophylline was observed. This increased in the order: III, I, II. Also the number of maximum increased, and in methanol solution the intensity of the strongest absorption bands increased in the same order. 21 references.

IT 6603-63-0, Theophylline, 2-thio-
(spectrum of)

RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1966:93480 CAPLUS Full-text

DOCUMENT NUMBER: 64:93480

ORIGINAL REFERENCE NO.: 64:17597b-h,17598a-e

TITLE: Syntheses in the purine series. XVII. Syntheses of
N,S-purinium betaines

AUTHOR(S): Brederick, Hellmut; Schellenberg, Peter; Nast, Roland;
Heise, Hartmut; Christmann, Otto

CORPORATE SOURCE: Tech. Hochsch., Stuttgart, Germany

SOURCE: Chemische Berichte (1966), 99(3), 944-57

CODEN: CHBEAM; ISSN: 0009-2940

DOCUMENT TYPE: Journal

LANGUAGE: German

OTHER SOURCE(S): CASREACT 64:93480

ED Entered STN: 22 Apr 2001

GI For diagram(s), see printed CA Issue.

AB cf. CA 57, 15107e. 7,9-Dimethyl- and 1,7,9-trimethyl-N,S-purinium betaines were prepared by the conversion of OH, SH, or PhCH₂S groups in 7,9-dimethyl- and 1,7,9-trimethylpurinium salts, resp., into the SH group and subsequent liberation from the resulting salts. Hypoxanthine (1.5 g.) in 15 g. p-MeC₆H₄-SO₃Me (I) stirred 15 min. at 250° and diluted with 25 cc. BuOH and then 150 cc. Et₂O yielded 2.3 g. 6-hydroxy-7,9-dimethylpurinium p-toluenesulfonate (II), m. 255-6° (BuOH). II (3.36 g.) and 80 cc. POCl₃ refluxed 2 hrs. and evaporated, treated with 125 cc. absolute EtOH and 7 g. CS(NH₂)₂ (III), refluxed 2 hrs., cooled, diluted with 400 cc. MeOH, and saturated with dry NH₃ yielded 1.14 g. pale yellow IV (R = H) (V), m. 283° (decomposition from 265° with sintering). 2-NH₂ derivative (3 g.) of II and 150 cc. POCl₃ refluxed 4 hrs., evaporated, treated with 200 cc. absolute EtOH and 10 g. III, refluxed 3.5 hrs., and saturated at 30-5° with dry NH₃ yielded 0.375 g. IV (R = NH₂) (VI), m. 312° (decomposition) with sintering from 295°. 2-MeS derivative (1.91 g.) of II and 60 cc. POCl₃, 60 cc. EtOH, and 5 g. III yielded similarly 0.81 g. IV (R = MeS) (VII), m. 277° (decomposition) with sintering from 265°. 7,9-Dimethylxanthinium p-toluenesulfonate (VIII), 125 cc. POCl₃, and 0.38 cc. H₂O refluxed 3.5 hrs. and then treated with 150 cc. absolute EtOH and 10 g. III followed by NH₃ gave 1.32 g. pale yellow IX (R = H) (X), m. 300°

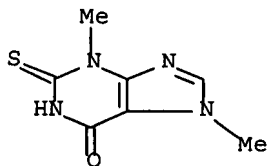
(decomposition) with sintering from 285°. 1-Me derivative (3.66 g.) of VIII gave similarly 0.64 g. XI (R = Me) (XII), m. 248° (MeOH). 2-Amino-6-mercaptapurine (0.5 g.) and 5 g. I stirred 10 min. at 117°, diluted with an equal volume EtOH, and treated dropwise with dry Et₂O gave 0.86 g. VII, m. 281°. VII (2.5 g.) added in portions with stirring to Cl in absolute MeOH gave 0.75 g. 2-amino-6-chloro-7,9-dimethylpurinium chloride (XIII), m. 293° (EtOH); picrate, m. 209° (EtOH). XIII (0.5 g.), 80 cc. absolute EtOH, and 0.5 g. III refluxed 4 hrs. yielded 0.32 g. pale yellow-green 6-SH analog (XIV) of XIII, m. 275°. XIV in MeOH treated with dry NH₃ gave VI. 6-Hydroxy-2-thioxodihydropurine (1.68 g.) in 0.4 g. NaOH in 50 cc. H₂O treated dropwise with stirring at room temperature during 1 hr. with 1.61 g. PhCH₂-Cl in 20 cc. MeOH and stirred 4 hrs. yielded 1.6 g. 6-hydroxy-2-benzylthiopurine (XV), m. 262-3° (absolute EtOH). XV (0.5 g.) and 5 g. I yielded 0.69 g. 6-hydroxy-2-benzylthio-7,9-dimethylpurinium p-toluenesulfonate (XVI), m. 240° (EtOH). 2,6-Dithioxotetrahydropurine (2.3 g.) in 250 cc. H₂O and 1.6 g. NaOH treated dropwise during 2 hrs. with 4.6 g. PhCH₂Br in 20 cc. MeOH and stirred 5 hrs. yielded 3.1 g. 2,6-bis(benzylthio)purine (XVII), m. 196° (absolute EtOH). XVII (2.5 g.) and 20 g. I stirred 10 min. at 170° yielded 2.02 g. 2,6-bis(benzylthio)-7,9-dimethylpurinium p-toluenesulfonate (XVIII), m. 170° (absolute EtOH). 2-Benzylthio-6-thioxo-1-methyl-dihydropurine (3 g.) and 20 g. I stirred 1 hr. at 150°, cooled, and diluted with 20 cc. absolute EtOH and 500 cc. Et₂O, and the oily precipitate treated in 500 cc. boiling H₂O with 10 cc. 65% HClO₄ yielded 2.4 g. 2-benzylthio-6-thioxo-1,7,9-trimethyl-dihydropurinium perchlorate (XIX), m. 177° (absolute EtOH). 2-Amino-6-benzylthiopurine (0.5 g.) and 5 g. I gave similarly after treatment of the product with 65% HClO₄ 0.56 g. 2-amino-6-benzylthio-7,9-dimethylpurinium perchlorate (XX), m. 226° (EtOH). XVI (0.5 g.), 2 g. AlBr₃, and 60 cc. dry MePh stirred 6 hrs. at 80° gave 0.16 g. XI (R = H) (XXI), m. 297° (H₂O). XVIII (1 g.), 4.0 g. AlBr₃, and 100 cc. dry MePh gave similarly 0.34 g. (crude) pale yellow XXII (R = H) (XXIII), m. 283° (decomposition) (H₂O). XIX (1 g.), 5 g. AlBr₃, and 150 cc. dry MePh yielded similarly 0.245 g. (crude) yellow XXII (R = Me) (XXIV), m. 255° (decomposition). XX (0.5 g.), 2 g. AlBr₃, and 60 cc. dry MePh gave 0.24 g. pale yellow 2-amino-6-mercapto-7,9-dimethylpurinium bromide, m. 270° (EtOH); a 0.5-g. portion in 25 cc. MeOH treated with dry NH₃ gave 0.31 g. VI, m. 312°. 6-Oxo-2-thioxo-3-methyltetrahydropurine (4.0 g.) in 250 cc. H₂O and 2.0 g. NaOH with 4.1 g. PhCH₂Br yielded 4.6 g. 2-benzylthio-6-oxo-3-methyl-dihydropurine (XXV), m. 218° (absolute EtOH). XXV (1.0 g.) and 5.0 g. I stirred 45 min. at 150°, and the oily product treated in 100 cc. BuOH with 3 cc. 65% HClO₄ and then 200 cc. Et₂O yielded 0.56 g. 2-benzylthio-6-oxo-3,7,9-trimethyl-dihydropurinium perchlorate (XXVI), m. 202° (absolute EtOH). XXVI (1.0 g.), 5.0 g. AlBr₃, and 150 cc. dry MePh yielded 0.45 g. (crude) 6-oxo-2-thioxo-3,7-dimethyltetrahydropurine, m. 308° (with sintering from 290°) (H₂O). V (0.200 g.) added in portions to 1 cc. 30% H₂O₂, and the sirupy product in 20 cc. MeOH treated successively with 0.5 cc. 30% H₂O₂ and dry NH₃ gave 0.115 g. 6-hydroxy-7,9-dimethylpurinium betaine (XXVII). Hypoxanthine (1.5 g.) in 15.0 g. I stirred 15 min. at 150° gave 2.3 g. 6-hydroxy-7,9-dimethylpurinium p-toluenesulfonate (XXVIII), m. 255-6° (BuOH). XXVIII (1.5 g.) in 150 cc. hot MeOH treated at room temperature with dry NH₃ gave 0.5 g. XXVII, m. 309°. XXVII (about 100 mg.) in 10-20 cc. MeOH treated with 5-6 drops 65% HClO₄ gave the perchlorate analog of XXVIII, m. 171° with sintering from 130° (BuOH). X.H₂O (0.400 g.) added in portions at 30° to 2 cc. 30% H₂O₂ and treated after 2 hrs. with dry NH₃ yielded 0.175 g. 7,9-dimethylxanthinium betaine (XXIX) (perchlorate, m. 281°), which was also obtained similarly from VII, XXI, and XXIII. 2-Hydroxy-6-thioxo-1-methyl-dihydropurine (3.64 g.) and 6.0 g. I in 25 cc. AcNMe₂ heated 15 min. at 145° gave 4.13 g. (crude) 2-hydroxy-6-thioxo-1,7,9-trimethyl-dihydropurinium p-toluenesulfonate; a 3.00-g. portion in 150 cc. MeOH treated at room temperature with concentrated NH₄OH yielded 0.85 g. 2-hydroxy-6-thioxo-1,7,9-trimethyl-dihydropurinium betaine (XXX), m. 355-7° (decomposition) (H₂O). The oxidation of XXX with H₂O₂ gave 1,7,9-trimethylxanthinium betaine (XXXa) which was also obtained from XII and XXIV.

VI oxidized similarly gave 2-amino-6-hydroxy-7,9-dimethylpurinium betaine (XXXI). The Rf values were determined with 2:1 BuOH-5N AcOH (A), 2:1 ProH-H₂O (B), 5% aqueous NH₄Cl (C), and 4% aqueous Na citrate (D), and the pKa, values in H₂O at 20° were measured potentiometrically or spectroscopically for the compds. listed in the table. The uv spectra of X, XII, XXI, XXIII, XXIV,XXX are recorded.Compound, A, B, C, D, pKa; V, 0.40, 0.60, 0.81, 0.80, 5.56 ± 0.04; VI, 0.41, 0.51, 0.66, 0.71, 6.28 ± 0.03; VII, 0.62, 0.75, 0.74, 0.66, 4.74 ± 0.08; X, 0.32, 0.50, 0.70, 0.65, 1.9 ± 0.2; XXX, 0.58, 0.72, 0.69, 0.66, 2.1 ± 0.2; XXI, 0.25, 0.41, 0.77, 0.73, 1.85 ± 0.2; XII, 0.42, 0.63, 0.79, 0.76, 1.95 ± 0.2; XXIII, 0.38, 0.57, 0.63, 0.58, 0.83 ± 0.13; XXIV, 0.57, 0.75, 0.57, 0.55, 0.71 ± 0.04; XXVII, 0.28, 0.50, 0.58, 0.87, --; XXXI, 0.30, 0.46, 0.81, 0.84, --; XXIX, 0.21, 0.38, 0.85, 0.76, --; XXXa, 0.40, 0.58, 0.90, 0.84, --; .

IT 19373-97-8P, Theobromine, 2-thio-
RL: PREP (Preparation)
(preparation of)

RN 19373-97-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,7-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1964:84708 CAPLUS Full-text

DOCUMENT NUMBER: 60:84708

ORIGINAL REFERENCE NO.: 60:14874c-e

TITLE: Action of 8-azaguanine and 8-azaxanthine on
Pseudomonas aeruginosa

AUTHOR(S): Bergmann, F.; Ungar-Waron, Hanna; Kwietny-Govrin,
Hanna

CORPORATE SOURCE: Hebrew Univ.-Hadassah Med. School

SOURCE: (1964), 91(2), 270-6

DOCUMENT TYPE: Journal

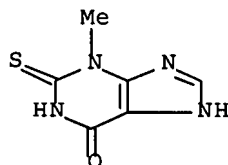
LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

AB 8-Azaguanine does not inhibit the growth of *P. aeruginosa*, but undergoes slow deamination. 8-Azaxanthine arrests the growth of this species temporarily. This growth retardation is abolished by hypoxanthine, xanthine, and a number of unnatural purines. During growth inhibition by azaxanthine, the xanthine oxidase-like activity of the bacterial cells is enhanced. Much larger increments of enzymic activity are obtained by the addition of hypoxanthine, xanthine, or certain unnatural purines, which all contain an unsubstituted imidazole ring. During growth inhibition by 8-azaxanthine, the urate oxidase-like activity of the bacteria is strongly depressed. On the other hand, the addition of hypoxanthine or xanthine to the culture medium produces a huge increase in the enzymic activity of the normal strain. After the 1st exposure to 8-azaxanthine a resistant strain emerges. This strain shows normal xanthine oxidase and urate oxidase activities, even when growing in the presence of the antimetabolite. Benzimidazole and benzotriazole are weak

growth inhibitors. They depress xanthine oxidase activity of the bacterial cells, but leave their urate oxidase activity unaffected.

IT 28139-02-8, Xanthine, 3-methyl-2-thio-
(effect on *Pseudomonas aeruginosa* response to 8-azaxanthine)
RN 28139-02-8 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1963:60954 CAPLUS Full-text

DOCUMENT NUMBER: 58:60954

ORIGINAL REFERENCE NO.: 58:10464a-e

TITLE: Relation of structure to the inhibitory activity of purines against urate oxidases

AUTHOR(S): Bergmann, F.; Kwietny-Govrin, Hanna; Ungar-Waron, Hanna; Kalmus, A.; Tamari, M.

CORPORATE SOURCE: Hebrew Univ.-Hadassah Med. School, Jerusalem

SOURCE: Biochemical Journal (1963), 86, 567-74

CODEN: BIJOAK; ISSN: 0264-6021

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

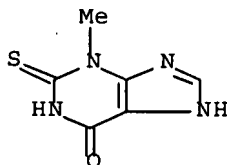
AB cf. *ibid.* 292. The inhibitory activity of a variety of compds. against urate oxidase has been determined: 150 values in μM were for hypoxanthine 220, 8-hydroxy-purine 110, 2-hydroxypurine 12, 2,8-dihydroxypurine 5.2, xanthine 18, 6,8-dihydroxypurine 66, 6-mercaptopurine 700, 6-thioxanthine 2.7, 2-thioxanthine 190, 8-hydroxy-6-mercaptopurine 70, 6-hydroxy-8-mercaptopurine 500, 6,8-dimercaptopyrine 370, 8-hydroxy-2-mercaptopurine 500, 2-hydroxy-8-mercaptopurine 12, 2-thiouric acid 250, 6-thiouric acid 14, 8-thiouric acid 5, 2,6-dithiouric acid 150, 2,8-dithiouric acid 80, 6,8-dithiouric acid 0.4, 6,8-dihydroxy-2-methylmercaptopurine 500, 2,6-dihydroxy-8-methylmercaptopurine 38, 2-hydroxy-6-methylmercaptopurine 6, 8-hydroxy-6-methylmercaptopurine 32, 2,8-dihydroxy-6-methylmercaptopurine 0.1,3, 8-hydroxy-3-methyl-6-methylmercapto-2-oxopurine 7, 4,5-diamino-6-thiouracil 38, 2,4-dihydroxypteridine 300, 2,4,6-trihydroxypteridine 150, 2,4,6,7-tetrahydroxypteridine 500, 8-aza-6-hydroxypurine 47, 8-aza-2-hydroxypurine 1.6, 8-azaxanthine 5.9, 3-methyl-2-thiouric acid 150, 3-methyl-6-thiouric acid 400, 3-methyl-8-thiouric acid 190, 3-methyl-2-thioxanthine 100, 3-methyl-6-thioxanthine 100, 7-methyl-6-thioxanthine 1000. The inhibitory effect was used to measure the affinity of the inhibitors for the enzyme. Of the 3 O atoms of uric acid, that of the 2-carbonyl group possesses the greatest binding power for the active center. Replacement of this O atom by S greatly diminishes the inhibitory activity. Combination of a 2-carbonyl group with S at C-6 enhances inhibitory activity considerably. On certain purine derivs., a 6-methylmercapto substituent is more effective than a 6-thiocarbonyl group. 2,6-Dihydroxy-6-methylmercaptopurine is the most potent inhibitor of urate oxidase known so far. Replacement of the imidazole moiety of the purine ring by triazole

enhances affinity, whereas introduction of the pyrazine ring, as in pteridines, greatly decreases it. Free imino groups are essential for the attachment of purines to urate oxidase, as N-methylation weakens or abolishes the inhibitory effect. On the other hand, in 2-thiopurines, methylation at N-3 increases the inhibitory power.

IT 28139-02-8, Xanthine, 3-methyl-2-thio-
(uric oxidase inhibition by)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 34 OF 47 CAPLUS . COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:436343 CAPLUS Full-text

DOCUMENT NUMBER: 57:36343

ORIGINAL REFERENCE NO.: 57:7262i,7263a-e

TITLE: Preparation and properties of 1,2-dihydrophthalazine derivatives

AUTHOR(S): Smith, Richard F.; Otremba, Edward D.

CORPORATE SOURCE: State Univ. Coll., Albany, NY

SOURCE: Journal of Organic Chemistry (1962), 27, 879-82

CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 57:36343

ED Entered STN: 22 Apr 2001

AB cf. CA 53:17143d. Reduction of 2-methyl-and 2-ethylphthalazinium iodide (I, II) with aqueous NaBH₄ yielded the corresponding 2-alkyl-1,2-dihydrophthalazines (III, IV). H₂O (3 l.) containing 0.3 mole o-HO₂CC₂H₄CHO stirred at 80° with 0.3 mole (N₂H₄)₂.H₂SO₄ and 1 l. 1.1 N NaOH, the green suspension evaporated in vacuo to 200 ml., extracted with C₆H₆, and the dried (MgSO₄) exts. evapd, yielded 50% phthalazine (V), m. 87-90°. Further extraction of the aqueous solution with EtOAc gave 0.9 g. 1(2H)-phthalazinone, m. 183-4°. I, m. 240-3° (decomposition), heated with saturated alc. picric acid (20 ml./g, halide) gave 75% picrate, m. 199-200° (decomposition). II, m. 225-8° (decomposition) (alc.), similarly yielded 93% II picrate, m. 167-9°. V (2 g.) and 4 ml. PhCH₂Cl refluxed 3 hrs. in 15 ml. dry MeOH, the cooled mixture diluted with anhydrous Et₂O, kept overnight, and the Et₂O-washed product dried in vacuo yielded 89% extremely hygroscopic 2-benzylphthalazinium chloride (VI), m. 175-8° (alc.-Et₂O); picrate m. 183-4° (MeOH). The powdered quaternary salts added portionwise to 3% aqueous NaBH₄ (3:1 salt-hydride), the cooled mixture extracted with Et₂O, the extract dried (MgSO₄), and the product isolated gave 2-alkyl-1,2-di-hydrophthalazines. Distillation yielded 75% III, b₁₇ 129-30°; HCl salt m. 133-5° (decomposition) (alc.); pierate m. 95-8° (decomposition); MeI salt (VII) m. 173-6° (MeOH). III on exposure to air rapidly yielded 2-methyl-1(2H)-phthalazinone, m. 108-10°. IV HCl salt, m. 142-4° (decomposition) (alc.), converted to the free base, refluxed 6 hrs. with excess MeI in alc., the resultant highly decompd, tarry product extracted

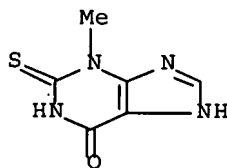
with EtOAc and the extract diluted with Et₂O gave IV MeI salt, m. 155-7° (alc.). VI (4.0 g.) reduced with aqueous NaBH₄, the oily product refluxed 3 hrs. with 7 ml. MeI in 25 ml. alc., and the mixture cooled gave 1.4 g. VII. Dilution of the filtrate c with Et₂O gave 1.4 g. unidentified material, m. 138-42°, recrystd. from alc.-Et₂O to give a sample, m. 140-2° (decomposition), melting with evolution of a potent lacrimator. VII (1 g.) in 10 ml. H₂O treated with 10 ml. 6N NaOH and the oily product extracted with Et₂O gave o-Me₂NCH₂C₄CN; picrate m. 144-5°; MeI salt m. 184-5°; HCl salt m. 226-7° (alc), v 2220 cm.⁻¹, identical with the salt prep'd, by stirring 0.05 mole each o-BrCH₂C₆H₄CN, Me₂NH.HCl, and anhydrous Na₂CO₃ 2 days at 20° in 50 ml. MeOH, acidifying the coned, solution with dilute HCl, basifying the Et₂O-washed aqueous layer, extracting with Et₂O, and treating the dried extract with anhydrous HCl.

IT 28139-02-8P, Xanthine, 3-methyl-2-thio-

RL: PREP (Preparation)
(preparation of)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:436342 CAPLUS Full-text

DOCUMENT NUMBER: 57:36342

ORIGINAL REFERENCE NO.: 57:7262h-i

TITLE: Condensed pyrimidine systems. XXII. N-methyl purines

AUTHOR(S): Elion, Gertrude B.

CORPORATE SOURCE: Burroughs Wellcome and Co. Inc., Tuckahoe, NY

SOURCE: Journal of Organic Chemistry (1962), 27, 2478-91

CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 57:36342

ED Entered STN: 22 Apr 2001

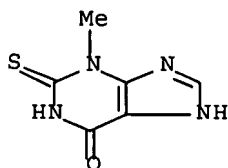
AB cf. CA 54, 18531b. A group of 1-and 3-monomethylpurines has been prepared by complete synthesis. Among the new derivs. are 3-methyladenine, 3-methylguanine, and the 1-and 3-methyl derivatives of 6-mercaptapurine. A number of 7- and 9-methyl derivs. have been obtained by direct methylation of 6-chloropurine, conversion to the mercapto derivs., and subsequent separation of the 7- and 9-methylpurine-6-thiols. Several ring openings and rearrangements have been observed in the course of attempts to prepare 1-methyladenine.

IT 28139-02-8P, Xanthine, 3-methyl-2-thio-

RL: PREP (Preparation)
(preparation of)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:429662 CAPLUS Full-text

DOCUMENT NUMBER: 57:29662

ORIGINAL REFERENCE NO.: 57:5924h-i,5925a-i,5926a-b

TITLE: The synthesis of some 6-thioxanthines

AUTHOR(S): Wooldridge, K. R. H.; Slack, R.

CORPORATE SOURCE: May Baker Ltd., Dagenham, UK

SOURCE: Journal of the Chemical Society (1962) 1863-28

CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 57:29662

ED Entered STN: 22 Apr 2001

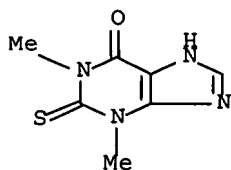
AB A series of 1,3- and 3,7-disubstituted 6-thioxanthines, of interest as broncho and coronary dilators, has been prepared by the selective thionation of the corresponding xanthines with P2S5 in C5H5N. 1,3,7-Trialkyl-6- thioxanthines could not be prepared in this way but were readily obtained from 1,3-dialkyl-6-thioxanthines. Theophylline (50 g.), 100 g. P2S3, and 1. dry C5H5N refluxed 8 hrs. with stirring, cooled, diluted with stirring during 1 hr. with 2 l. H2O, concentrated to about 1/3 volume, cooled, and filtered, and the residue dissolved in 2N NaOH, filtered, and reprecipitated with dilute HCl yielded 51 g. 1,3-dimethyl-6-thioxanthine (I), pale yellow needles, m. 323-5° (decomposition) (EtOH or H2O). 6-Thiotheobromine (75 g.) with 150 g. P2S5 gave similarly 72 g. 3,7-dimethyl-6-thioxanthine (II), m. 300-1°. (MeNH)2CS (79 g.) added in portions with stirring during 0.5 hr. to 65 g. NCCH2CO2H in 156 g. Ac2O and 200 cc. AcOH at 65°, kept 2 hrs. at 65° evaporated at 69-5° in vacuo, and the gummy residue stirred at 50° with 200 cc. H2O and adjusted to pH 10 with 50% aqueous NaOH gave 65 g. 6-amino-1,3-dimethyl 2-thiouracil (III), prisms, m. 286-8° (EtOH). The crude III suspended in 6000 cc. H2O containing 25.5 g. NaNO2 at 80-90°, 50 cc. AcOH added during 15 min., and the mixture stirred 15 min. at 80-90° and cooled yielded crude 5-NO derivative (IV) of III, blue-green amorphous solid, m. 215-16° (decomposition). The IV added in 5-g. portions to 2.5 l. H2O at 70-80° together with sufficient Na2S2O4 to discharge the color of the IV, cooled, and filtered, the residual 5-NH2 derivative of III, m. 230-4°, added immediately to 500 cc. 2N H2SO4, the resulting sulfate (57 g.) boiled 0.5 hr. with 500 cc. HCONH2, diluted with 250 cc. H2O, and cooled, and the yellow solid dissolved in 300 cc. hot 17% NH4OH, filtered, and acidified to pH 4 with AcOH yielded 47 g. 1,3dimethyl-2-thioxanthine, m. 344-8°. Me2SO4 (25.2 g.) added dropwise in 15 min. with stirring at 40° to 35 g. I and 100 cc. 2N NaOH, kept 0.5 hr. at 40°, cooled, and filtered gave 15 g. 1,3,7-trimethyl-6-thioxanthine (V), pale yellow prisms, m. 246-7°. II (17.5 g.) and 42.5 g. Me2SO4 gave 1 g. V, m. 247-9°. II(10g.) in 125 cc. 0.5N NaOH stirred 2 hrs. at room temperature with 10.7 g. MeI yielded 6.7 g. 1,2,3,4tetrahydro-3,7-dimethyl- 1-methylthiopurine, needles, m. 300-3° (H2O). The appropriate urea was converted by the method of Traube [Ber. 33, 3035(1900)] or of Speer and Raymond (CA 48, 1346h) or of Montgomery (CA 50,

13932b) to the corresponding 1,3-dialkylxanthines (1- and 3-alkyl group and m.p. given): Me, MeO(CH₂)₃, 166-8°; Me, furfuryl, 255-8°; Et, iso-Bu, 195-7°; Pr, iso-Bu, 189-92°; Bu, Me, 207-10°. Similarly were prepared 3-isobutylxanthine (VI), m. 299-301°, and the 7-Me derivative of VII, m. 239-41°. P2S5 (600 g.) and 482 g. 3-isobutyl-1-methylxanthine in 4.2 l. dry C₅H₅N, refluxed 9 hrs. with stirring, cooled to about 40°, diluted carefully with H₂O, concentrated to about 2.5 l., diluted with 3.5 l. H₂O, and filtered, and the residue dissolved in 2.5 l. warm N NaOH, filtered, and acidified with concentrated HCl to pH 4 pp.d. 426 g. 3-isobutyl-1-methyl-6-thioxanthine (VII), yellow prisms, m. 170-2° (EtOH). Similarly were prepared the following 1,3-disubstituted-6-thioxanthines (1- and 3-substituent, m.p., and % yield given): Me, Me (VIII), 3235°, 94; Me, Et, 235-7°, 79; Me, Pr, 164-7°, 63; Me, Bu, 156-8°, 73; Me, Am, 169-70°, 50; Me, C₆H₁₃, 167-74°, 78; Me, iso-Am, 156-60°, 50; Me, MeO(CH₂)₃, 150-2°, 50; Me, CH₂:CHCH₂, 152-6°, 81; Me, CH:CMech₂, 195-8°, 47; Me, PhCH₂, 213-15°, 84; Me, Ph(CH₂)₂, 198-9°, 63; Me, furfuryl, 184-6°, 15; Et, Me, 235-9°, 76; Et, Et, 2568°, 72; Et, Bu, 175-8°, 74; Et, iso-Bu, 180-3°, 39; Et, CH₂:CHCH₂, 210-12°, 49; Pr, Pr, 212-15°, 89; Bu, Me, 295-8°, 84; Bu, Bu, 183-6°, 72. Similarly were prepared the following 8-substituted VIII (substituent, m.p., and % yield given): Me, 294-5°, 75; Et, 218-19°, 76; SH, 240° (decomposition), 83. I (42 g.) and 8.6 g. NaOH in 150 cc. H₂O stirred 0.5 hr. at room temperature, cooled, and filtered, and the dried Na salt (44 g.) of I dissolved in 200 cc. HCONMe₂, treated with stirring during 15 min. at room temperature with 18.6 g. AcCH₂Cl, stirred 0.5 hr., diluted with 300 cc. iced H₂O, and filtered gave 21.3 g. 7-AcCH₂ derivative (IX) of I, yellow needles, m. 208-10°. IX (21 g.), 269 g. paraformaldehyde, 11.9 g. piperidine-HCl, 1.6 cc. Et₂O.BF₃, and 200 cc. dry dioxane stirred 7 hrs. at 100° and filtered gave 23.0 g. 1,3-dimethyl-7(2-oxo-4-piperidinobutyl)-6-thioxanthine-HCl, yellow-brown prisms, m. 197-200°. In the same manner as VII were prepared the following 1,3,7-trisubstituted-6-thioxanthines (1-, 3-, and 7-substituents and m.p. given): Me, Me, Et, 22830°; Me, Me, Et₂N(CH₂)₂, 52-4°; Me, iso-Bu, Et₂N(CH₂)₂ [isolated as the (-)-di(p-toluoyl) D-tartrate], 120° (decomposition); Me, iso-Bu, AcCH₂, 170-4°; Bu, Me, Me, 118-19°. In the same manner were prepared the following 3,7-dialkyl-6thioxanthines (3- and 7-substituents and m.p. given): Me, Me, 300-1°; Bu, Me, 200-3°; iso-Bu, Me, 228-30°. Also prepared was 3-methyl-6-thioxanthine, m. 269-74°. Choline chloride (3.4 g.) in 900 cc. hot iso-PrOH treated with stirring with 150 g. 85% KOH in 600 cc. absolute MeOH, cooled to 0°, filtered, treated with 500 g. VII, warmed a few min., and evaporated in vacuo, the residual sirup dissolved in 1 l. hot iso-PrOH, treated with C, filtered, diluted with 1 l. dry Et₂O, and cooled, and the precipitated filtered off gave 548 g. choline salt of VII, pale yellow prisms, m. 145-9°; their mother liquor evaporated, and the sirupy residue dissolved in H₂O and acidified to pH 4 with HCl gave 8 g. VII. Similarly were prepared the choline salts of the following 1,3-disubstituted-6-thioxanthines (1- and 3-substituents, m.p. and % yield given): Me, Me (X), 145-7°, 47; Me, Et, 157-9°, 72; Me, Pr, 145-50°, 72; Me, Bu, 133-5°, 88; Me, Am, 150-3°, 93; Me, C₆H₁₃, 55-7°, 94; Me, iso-Bu, 148.5-9.5°, 92; Me, iso-Am, 125-8°, 90; Me, CH₂:CHCH₂, 172-5°, 73; Me, CH₂:CMech₂, 145-51°, 80; Me, PhCH₂, 166-71°, 80; Me, Ph(CH₂)₂, 173-5°, 80; Et, Me, 157-8°, 70; Et, Et, 142-7°, 92; Et, Bu, 115-18°, 79; Pr, Pr, 114-18°, 57; Bu, Me, 105-9°, 62. Also prepared were 8-Me derivative of X, 175-6°, 65, and the 8-SH derivative of X, 209 11°, 70. The ultraviolet absorption maximum of a number of thioxanthines are tabulated.

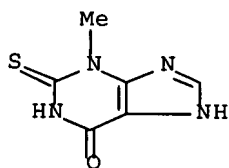
IT 6603-63-0P, Theophylline, 2-thio-
 RL: PREP (Preparation)
 (preparation of)

RN 6603-63-0 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1962:418827 CAPLUS Full-text
 DOCUMENT NUMBER: 57:18827
 ORIGINAL REFERENCE NO.: 57:3862h-i,3863a
 TITLE: Specific reactions of the purine-oxidizing system of *Pseudomonas aeruginosa*
 AUTHOR(S): Bergmann, Felix; UngarWaron, Hanna; Kwietny-Govrin, Hanna; Goldberg, Hilda; Leon, Shalom
 CORPORATE SOURCE: Hebrew Univ., Jerusalem, Israel
 SOURCE: Biochimica et Biophysica Acta, Specialized Section on Nucleic Acids and Related Subjects (1962), 55, 512-22
 CODEN: BBASB7; ISSN: 0926-6550
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 22 Apr 2001
 AB cf. CA 55, 26059g. Resting cells of *P. aeruginosa* oxidized 2-aminopurine and its MeNH- and Me2N- analogs at C-8 in contrast to the action of mammalian xanthine oxidase. 6-Mercaptopurine was attacked 1st at C-2, then at C-8, and then further. This compound did not inhibit growing *P. aeruginosa*, but increased production of xanthine oxidase. The 3-Me derivs. of thioxanthines were oxidized at C-8, while 3methylhypoxanthine was first attacked at C-2. The resulting complex, containing 3-methylxanthine, dissociated before further oxidation to 3-methyluric acid, in contrast to xanthine. The results are discussed in reference to the mechanism of attack and the different actions of bacterial and mammalian xanthine oxidases. 21 references.
 IT 28139-02-8, Xanthine, 3-methyl-2-thio-
 (oxidation by xanthine oxidase of *Pseudomonas aeruginosa*)
 RN 28139-02-8 CAPLUS
 CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1962:410979 CAPLUS Full-text
 DOCUMENT NUMBER: 57:10979
 ORIGINAL REFERENCE NO.: 57:2268g-i,2269a-i,2270a-c
 TITLE: Alkaloids of *Tylophora crebriflora*-structure and

synthesis of tylocrebrine, a new phenanthroindolizidine alkaloid

AUTHOR(S): Gellert, E.; Govindachari, T. R.; Lakshmikantham, M. V.; Ragade, I. S.; Rudzats, R.; Viswanathan, N.

CORPORATE SOURCE: Univ. N. S. W., Sydney

SOURCE: Journal of the Chemical Society (1962) 1008-14
CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

AB Milled *T. crebriflora* (21 lb.) extracted with hot MeOH, the extract concentrated to small volume (4 l.), diluted with 2 l. H₂O, concd, to 800 ml. in a climbing film evaporator, and the mixture filtered while warm gave a solid (I) and a filtrate (II). II acidified with dilute AcOH, extracted exhaustively with CCl₄, the combined CCl₄ solns, extracted with 2N HCl, the extract combined with the previous acidic phase, and filtered gave a filtrate (III), which gave a strong Mayer test and showed 2 fluorescent spots when chromatographed on paper in BuOH-AcOH (R_f 0.2 and 0.5). I in warm 2N AcOH diluted with hot H₂O, cooled, filtered, the filtrate extracted with CCl₄, combined with III, made basic with concd, aqueous, the precipitate (45 g.) repeatedly precipitated from hot aqueous AcOH with concd, aqueous NH₃, extracted (Soxhlet) with MeOH, and the product crystd, from MeOH gave crude alkaloid mixture (IV). Crude IV (in 2 g. batches) subjected to partition chromatography in 15:85 PrOH-2N-AcOH on a cellulose column (partial separation into fractions with R_f 0.2 and 0.5), the fractions from several such chromatograms combined (intermediate fractions were rechromatographed), the 1st fraction evaporated in vacuo, the residue dissolved in warm dilute AcOH, made alkaline with concd, aqueous NH₃ and the crude alkaloid [R_f 0.5 (in 3:97 AcOH-BuOH saturated with H₂O) (solvent A)] crystallized 3 times from MeOH gave tylocrebrine (V), m. 218-20° (decomposition), λ 263, 342, and 360 m μ (ϵ 4.81, 3.25, and 3.09), $[\alpha]_{24D}$ -45 \pm 2° (c 0.74, CHCl₃), pK_a 6.7 (in 50% aqueous EtOH) [HI salt m. 214-17° (decomposition) (aqueous MeOH); perchlorate m. 262-4° (decomposition); picrate m. 134-6° (Me₂CO containing a little MeOH)]. The crude alkaloid [R_f 0.2 (solvent A)] from the 2nd fraction recrystd. 3 times from CHCl₃-MeOH gave tylophorine (isomeric with V), m. 282-4° (decomposition), λ 257, 290, 340, 355 m μ (ϵ 4.82, 4.51, 3.43, 2.96). V refluxed on a H₂O bath with excess MeI in MeOH until dissolved, then refluxed 30 min. more, concentrated, and cooled gave optically active V.MeI, m. 255-8° (decomposition) (MeOH), $[\alpha]_{21D}$ -30 \pm 2° (c 0.30, MeOH). Optically active V.MeI refluxed 30 min. in 20% aqueous NaOH gave (\pm)-V.MeI, m. 264-6° (decomposition) (MeOH), $[\alpha]_{21D}$ 0° (c 0.10, MeOH). V.MeI (1.4 g.) refluxed with AgCl in aqueous MeOH, the resulting V.MeCl shaken with Ag₂O in H₂O, the solution of V.MeOH evaporated to dryness, the residue heated 3 min. at 240°/0.2 mm., and the product chromatographed in C₆H₆ on basic Al₂O₃ gave 400 mg. VI, m. 144.5-5.0° (C₆H₆-petr. ether, then petr. ether). V.MeI (100 mg.) converted directly into V.MeOH (with Ag₂O in 10 ml. H₂O; 5 hr.), the mixture filtered, the filtrate evaporated in vacuo at 50° the residue heated 30 min. at 100°/0.05 mm., the product repeatedly extracted with hot C₆H₆, and chromatographed in C₆H₆ on Al₂O₃ gave 10 mg. VI, m. 144.5-5.0°. VI (50 mg.) in 3 ml. AcOH heated 5 min. at 125° with excess HIO₄ gave no CH₂O (no precipitate with dimedon). Et 3,4,6,7-tetramethoxyphenanthrene-9-carboxylate (3 g.) in 25 ml. dry tetrahydrofuran added to 1.5 g. LiAlH₄ in 15 ml. tetrahydrofuran with stirring, stirred 4 hrs., treated with Et₂O and H₂O, the organic layer decanted, and evaporated gave 2.2 g. 9-hydroxymethyl-3,4,6,7-tetramethoxyphenanthrene (VII), m. 164-5° (C₆H₆). VII (5 g.), 4 ml. SOCl₂, and 0.5 ml. pyrldine in 120 ml. CHCl₃ heated 15 min. at 40-60°, cooled, poured into H₂O, extracted with CHCl₃, the extract dried, concentrated to small volume, and diluted with petr. ether gave 4.2 g. 9-chloromethyl-3,4,6,7-tetramethoxyphenanthrene (VIII), m. 148° (decomposition) (C₆H₆-petr. ether).

VIII (4 g.) in 40 ml. dry tetrahydrofuran added dropwise with stirring to pyrrolmagnesium bromide (from 1.8 g. Mg, 5.8 ml. EtBr, and 5.26 ml. freshly distilled pyrrole) in Et₂O cooled in ice under N, stirred 3 hrs. during which the mixture was allowed to reach room temperature, diluted with Et₂O, decomposed with saturated aqueous NH₄Cl, the organic layer separated, washed with H₂O, dried, evaporated, and the residue chromatographed in CHCl₃ on Al₂O₃ gave 2 g. 2-(3,4,6,7-tetramethoxy-9-phenanthrylmethyl)pyrrole (IX), m. 155-6° (C₆H₆-petr. ether). IX (0.4 g.) in 30 ml. AcOH containing 0.25 g. PtO₂ hydrogenated 8 hrs. at room temperature at 60 lb./sq. in., filtered, the filtrate evaporated in vacuo, the residue extracted repeatedly with hot dilute HCl, the combined exts. basified with aqueous NH₃, and the product isolated with CHCl₃ gave 0.25 g. corresponding pyrrolidine (X), oil; picrate m. 247-9° (AcOH). X (0.5 g.) and 3 ml. 98% HCO₂H heated 1.5 hrs. at 180°, cooled, dissolved in CHCl₃, the solution washed, dried, evaporated, the residual N-formyl derivative refluxed 1.5 hrs. with 4 ml. POCl₃ and 15 ml. PhMe, the solution mixture cooled, diluted with petr. ether, the resulting quaternary chloride dried in vacuo, reduced with 0.8 g. NaBH₄ in 30 ml. MeOH, the solution evaporated in vacuo, the residue taken up in CHCl₃, the solution washed with H₂O, dried, evaporated, and the residue chromatographed in CHCl₃ on Al₂O₃ gave 0.2 g. (±)-V, m. 219-21° (CHCl₃-MeOH). (±)-V (200 mg.) in 10 ml. CHCl₃ refluxed 3 hrs. on a H₂O bath with 2 ml. MeI and kept overnight at 30°, the solution evaporated, the resulting (±)-V.MeI shaken 5 hrs. with Ag₂O (from 1 g. AgNO₃) and 10 ml. H₂O, and the (±)-V.MeOH subjected to Hofmann degradation as above gave 40 mg. VI, m. 144.5-5.0° (C₆H₆-petr. ether). 2-Amino-α-(3,4-dimethoxyphenyl)-4,5-dimethoxycinnamic acid (G. et al., loc. cit.) diazotized in Me₂CO with BuONO and subjected to Pschorr ring closure gave 2,3,5,6-tetramethoxyphenanthrene-9-carboxylic acid (XI). XI (5 g.) refluxed 4 hrs. with 4 ml. concentrated H₂SO₄ in 150 ml. MeOH gave 4.2 g. Me ester of XI, m. 150° (EtOH). XI was converted successively as above into 9-hydroxymethyl-2,3,5,6-tetramethoxyphenanthrene, m. 133° (C₆H₆); 9-chloromethyl-2,3,5,6-tetramethoxyphenanthrene, m. 163-4° (C₆H₆-petr. ether); 2-(2,3,5,6-tetramethoxy-9-phenanthrylmethyl)pyrrolidine [picrate m. 218° (decomposition) (AcOH-EtOH)]; and finally 9,11,12,13,13a, 14-hexahydro3,4,6,7-tetramethoxydibenzo [f,h] pyrrolo [1,2-b] isoquinoline (XII), m. 219° (CHCl₃-MeOH). XII (200 mg.) converted to the methiodide and the product subjected to the Hofmann degradation as above gave 30 mg. XIII, m. 137-8° (C₆H₆-petr. ether). The structure of V is shown.

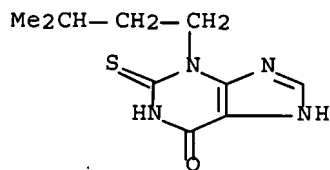
IT 94689-49-3P, Xanthine, 3-isopentyl-2-thio-

RL: PREP (Preparation)

(preparation of)

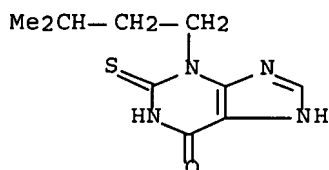
RN 94689-49-3 CAPLUS

CN Xanthine, 3-isopentyl-2-thio- (7CI) (CA INDEX NAME)



Serial No.: 10/511,537

TITLE: Synthesis of Dihydrotriacanthine
AUTHOR(S): Leonard, Nelson J.; Laursen, Richard A.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Journal of Organic Chemistry (1962), 27, 1778-80
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB 3-Isopentyladenine was synthesized and shown to be identical with dihydrotriacanthine.
IT 94689-49-3P, Xanthine, 3-isopentyl-2-thio-
RL: PREP (Preparation)
(preparation of)
RN 94689-49-3 CAPLUS
CN Xanthine, 3-isopentyl-2-thio- (7CI) (CA INDEX NAME)



L9 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:410977 CAPLUS Full-text
DOCUMENT NUMBER: 57:10977
ORIGINAL REFERENCE NO.: 57:2267f-i,2268f-g
TITLE: Synthesis of calycotomine and its analogs
AUTHOR(S): Chatterjee, A.; Chaudhury, N. Aditya
CORPORATE SOURCE: Univ. Coll. Sci., Calcutta
SOURCE: Journal of Organic Chemistry (1962), 27, 309-10
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB cf. CA 54, 22693g. Liquid NH₃ (300 ml.) containing 8.73 g. Na treated with a thin stream of 22.0 g. 3,4-(MeO)2C₆H₃CH₂CH₂NH₂ and the mixture kept 6 hrs. with rise of temperature to 30° decompd, by cautious addition of ice and washed twice with 50 ml. Et₂O, the aqueous phase aerated and the NH₃-free soln. acidified with AcOH with cooling, washed with Et₂O and made alkaline with NaHCO₃, extracted 3 times with 100 ml. BuOH and the dried extract (150 ml.) treated with HCl in Et₂O yielded 18.0 g. 3,4-HO(MeO)C₆H₃CH₂CH₂NH₂.HCl (I), m. 203-4° (absolute alc.Et₂O). I (0.9 g.) and 0.4 g. HOCH₂CHO in 10 ml. H₂O adjusted to pH 4.,5-5.0 and kept 3 days at 30° basified with Na₂CO₃ and extracted with CHCl₃ gave 0.6 g. 6-demethylcalycotomine (II, R₁ = OH, R₂ = OMe) (III), m. 198-200° (decomposition). III (0.6 g.) in 50 ml. dry Et₂O added slowly to CH₂N₂ [from Me(NO)NCONH₂] and kept 16 hrs. at 28-6° before evapn, in vacuo, the residue (0.5 g.) taken up in 20 ml. 4N HCl and washed 3 times with 25 ml. Et₂O, the acidic aqueous solution basified with 45 ml. 10% aqueous NaOH and extracted 3 times with 50 ml. CHCl₃ yielded 45-50% dl-calycotomine (II, R₁ = R₂ = OMe), m. 134° (1:1 EtOAc-petr. ether), λ 240, 290 mμ (log ε 3.48, 3.66, alc.); HCl salt m. 195-6° (absolute alc.-Et₂O). Concentrated HCl (8 ml.) heated 8 hrs. with 5.0 g. 3,4-(MeO)2C₆H₃CH₂CH₂NH₂ at 160-70° in a sealed tube and the product cooled in an ice bath yielded 4.0 g.

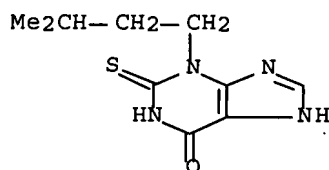
3,4-(HO)2C6H3CH2NH2HCl (IV), m. 241° (Me2CO). IV (1.0 g.) and 0.6 g. HOCH2CHO in 10 ml. H2O adjusted to pH 3-4 and kept 3 days at 25-6°, concd, in vacuo and the cryst, product recrystd, from 1: 1 alc.-Me2CO gave 0.85 g. 6,7-demethylcalycotomine (II, R1 = R2 = OH), m. 208-9° (decomposition), λ 288 m μ (log ϵ 3.57). Condensation of 0.08 g. with 0.15 g. 3,4-(HO)2C6H3CH2CH(NH2)CO2H.HCl in 5 ml. H2O at pH 4-5 gave 0.1 g. 3-carboxy-6,7-demethylealycotomine, m. 281-2° (decomposition), λ 280 m μ (log ϵ 3.54).

IT 94689-49-3P, Xanthine, 3-isopentyl-2-thio-

RL: PREP (Preparation)
(preparation of)

RN 94689-49-3 CAPLUS

CN Xanthine, 3-isopentyl-2-thio- (7CI) (CA INDEX NAME)



L9 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:25096 CAPLUS Full-text

DOCUMENT NUMBER: 56:25096

ORIGINAL REFERENCE NO.: 56:4762b-h

TITLE: Synthesis and properties of 3-methylpurines

AUTHOR(S): Bergmann, Felix; Levin, Gershon; Kalmus, Abraham;
Kwietny, Hanna

CORPORATE SOURCE: Hebrew Univ.-Hadassah Med. School, Jerusalem, Israel

SOURCE: Journal of Organic Chemistry (1961), 26, 1504-8

CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

AB A series of substituted purines was prepared and, by comparison of their ultraviolet spectra, it was deduced that 3-methylhypoxanthine (I), 8-hydroxy-3-methyl-6-purinone (II), 3-methyl-8 hydroxypurine (III), 3-methylpurine-6-thione (IV), and 3-methyl-6-methylthiopurine (V) had C:N bonds fixed in the 1,2-position. This bond fixation alone was inadequate in explaining the rate of attack of these compds. by milk xanthine oxidase. 3-Methylxanthine (3 g.) was refluxed 2 hrs. with 15 g. P2S5 in 150 ml. C5H5N, the solvent evaporated, the residue heated with water (15 min.), and the pH brought to 9 with NH4OH. After 30 min., this solution was filtered, and the filtrate concentrated in vacuo to 50 ml. and acidified to pH 5.5 to precipitate 2.2 g. 2-hydroxy-3-methylpurine-6-thione (VI), which was purified by treatment with C in 5% NaOH, precipitated with HOAc, and recrystd. from water as yellow needles, decomposing above 300°. VI (1.2 g.) in 25 ml. N NaOH was refluxed 2 hrs. with 4 g. Raney Ni (VII), VII removed, and the solution evaporated to dryness. The residue was dissolved in 5% ethanolic H2SO4 and water added to just clarify the solution which, after treatment with C and storage at 0°, deposited 23% 3-methyl-2-purinone (VIII) as the sulfate in large colorless plates. VIII, colorless needles, decomposed 297-300° (EtOH). Similarly, 0.2 g. 3-methyl-6-thiouric acid refluxed 70 min. with 0.8 g. VII in 20 ml. 5% NH4OH gave, on acidification and cooling, 90 mg. 8-hydroxy-3-methyl-2-purinone, flat rods, decomposing above 300° (water). 1,2-Dihydro-1-methyl-2-thio-4-hydroxy-5,6-

diaminopyrimidine (IX) (CA 55, 2656g) (3.3 g.) and 12 ml. HCONH₂ heated 1.5 hrs. at 180-90° gave, on cooling, 3.2 g. 6-hydroxy-3-methylpurine-2-thione (X), prisms, decomposing above 300° (water). X (3 g.) was heated to 90° in 70 ml. 5% NH₄OH, 9 g. VII added, and heating and stirring continued 2 hrs. to give, on cooling and concentration of the solution, 1.9 g. I, colorless needles, decomposing above 300° (50% EtOH) (crystallizing with 1/3 H₂O). Heating 1 g. IX and 1 g. CO(NH₂)₂ 20 min. at 195°, dissolving the product in 5% NaOH, treating with C, and acidifying with 20% H₂SO₄pptd. 90% 6,8-dihydroxy-3-methylpurine-2-thione (XI), decomposing above 300°.

Desulfurization of XI in 10 ml. N NaOH (refluxed 1.5 hrs. with 1.5 g. VII) followed by acidification with 20% H₂SO₄ gave 0.3 g. II, colorless plates, decomposing above 300° (H₂O). 2,6-Dimercapto-3-methyl-8-purinol (1 g.) in 10 ml. 2.5% NaOH was refluxed with stirring with 2 g. VII; after 45 min., 2 g. VII was added and refluxing continued 70 min. The filtrate was brought to pH 7.5 with HOAc, evaporated to dryness, and the residue extracted with cold EtOH. The residue was crystallized from hot 90% EtOH to give 250 mg. III, subliming about 250°, m. above 300°. Treatment of 0.8 g. XI with 2.5 g. P₂S₅ in 45 ml. C₅H₅N (as in the preparation of VI) gave 68% 2-mercapto-3-methylpurine-6-thione (XII), yellowish elongated prisms, decomposing above 300° (Me₂NCHO-water). Refluxing 1.1 g. I with 5 g. P₂S₅ in 60 ml. C₅H₅N 4 hrs. gave, after evaporation of solvent and treatment with hot water, 0.8 g. IV, yellowish pointed prisms, decomposing above 300° (H₂O). Treatment of 0.4 g. IV in 5 ml. 2.5% NaOH at room temperature with 0.3 ml. MeI (2 hrs.) gave 0.4 g. V, colorless prisms (water), m. 166°. IV, V, and XII could not be desulfurized to 3-methylpurine.

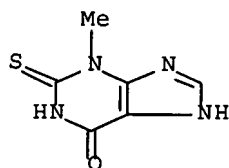
IT 28139-02-8P, Xanthine, 3-methyl-2-thio-

RL: PREP (Preparation)

(preparation of)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:18329 CAPLUS Full-text

DOCUMENT NUMBER: 56:18329

ORIGINAL REFERENCE NO.: 56:3480c-i,3481a-b

TITLE: Synthesis of 8-substituted purines

AUTHOR(S): Bergmann, F.; Tamari, M.

CORPORATE SOURCE: Hebrew Univ., Jerusalem, Israel

SOURCE: Journal of the Chemical Society (1961) 4468-72

CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 56:18329

ED Entered STN: 22 Apr 2001

AB Condensation of an acetamidine salt with an appropriate derivative of 4,5-diaminopyrimidine in the absence of a solvent led directly to high yields of

the 8-substituted purines (I). General procedure. A mixture of a 4,5diaminopyrimidine and 2 equivs. MeC(:NH)NH₂.HCl (II.HCl) heated to 180-90° (homogeneous melt was formed and NH₃ was evolved), when reaction ceased, the melt dissolved in N NaOH, the solution decolorized with C, and acidified with AcOH to pH 6 gave the I, all decomposing above 310° [substituents at 2-, 6-, and 8-position, reaction time in min., % yield, λ (mμ) at pH 8.0, R_f in 85:10:5 95% EtOH-H₂OAcOH (solvent A), 70:20:10 95% EtOH-pyridine-H₂O (solvent B), and 65:25:10 iso-PrOH-HCONMe₂-10% aqueous NH₃ (solvent C) given]: H, OH, Me, 60, 56 (the yield was improved by addition of 2 equivs. anhydrous NaOAc), 2.52, 0.57, 0.70, --; H, OH, Me, 60, 67 (with II.AcOH), --, --, --, --; OH, OH, Me, 30, 94, 240 and 275, 0.54, 0.60, 0.42; OH, SH, Me (III), 35, 83 (the yield was improved by addition of 2 equivs. anhydrous NaOAc) (the same compound was also prepared in 90% yield from 8-methylxanthine with P₂S₅), 251 and 344, 0.50, 0.56, 0.57; SH, OH, Me, 30, 77, 235 and 280, 0.45, 0.74, 0.61; SH, SH, Me, 25, 65 (the yield was improved with 2 equivs. anhydrous NaOAc), 247 and 285, and 351, 0.53, 0.59, 0.71; SH, SH, Me (IV), 25, 86 (with II.AcOH), --, --, --, --; SH, NH₂, Me (V), 30, 66 (isolated as the sulfate), 230 and 251, and 280, 0.61, 0.67, --; H, OH, Ph, 70, 50, 291, 0.58, 0.79, --; H, OH, Ph, 70, 78 (with II.AcOH), --, --, --; OH, OH, Ph, 40, 80, 228 and 309, 0.52, 0.66, --. Also were prepared 92% 3,8-dimethylxanthine (VI), λ (pH 8.0) 275 m, R_f 0.64 (in A), 0.79 (in B), and 0.68 (in C), and 88% 3,8-dimethyl-2-mercaptioxanthine (VII), λ (pH 8.0), 233 and 288 mμ, R_f 0.60 (in A) and 0.84 (in B). N:C(OH).-N:C(NH₂).C(NH₂):CH (VIII) (Kalmus and Bergmann, CA 55, 12418h) (1 g.), 1 g. II.HCl, and 0.8 g. anhydrous NaOAc heated 20 min. at 140-5, the resulting cake dissolved in 10% aqueous NH₃, the solution boiled with C, filtered, and the filtrate kept 24 hrs. in a cold room gave 0.65 g. inseparable mixture of VIII and 2-hydroxy-8-methylpurine (IX), (pH 8.0) 307 m. III (5 g.) and 1.5 g. (wet weight) Raney Ni in 25 ml. 5% aqueous NH₃ refluxed 80 min., filtered, the filtrate adjusted to pH 2 with HNO₃, and kept 2 months at room temperature gave IX.HNO₃. If the above ammoniacal solution was acidified with H₂SO₄, IX decomposed quant. The same result was obtained when an ammoniacal solution of IX was evaporated to dryness, the residue extracted with absolute EtOH, and the mixture acidified with 1% alc.-H₂SO₄. V (580 mg.) and 1.5 g. (wet weight) Raney Ni in 100 ml. 5% aqueous NH₂ refluxed 2 hrs., filtered hot, and the filtrate cooled gave 300 mg. 8-methyladenine, R_f 0.57 (in A), 0.67 (in B), and 0.64 (in C). 8-Methylhypoxanthine (1.3 g.), 5 g. P₂S₅, and 50 ml. dry pyridine refluxed 4 hrs., concentrated in vacuo, the residue extracted with 37 NaOH, filtered, the solution concentrated in vacuo, and kept overnight at 0° gave 1.1 g. 6-mercapto-8-methylpurine, decomposed above 310° (H₂O), (pH 8.0) 232 and 316 m, R_f 0.64 (in A) and 0.71 (in C). VII (1 g.) and 0.7 ml. MeI stirred 30 min. at room temperature in 10 ml. 0.5N NaOH gave 0.95 g. 3,8-dimethyl2-(methylthio)hypoxanthine, decomposed at 312-15° (H₂O), R_f 0.73 (in B). VII (2 g.) and 6 g. (wet weight) Raney Ni in 50 ml. 5% aqueous NH₃ refluxed 2 hrs., filtered, and concentrated in vacuo gave 1.4 g. 3,8-dimethylhypoxanthine, decomposed at 300° (EtOH), R_f 0.6 (in B). NH.CO.NMe.C(NH₂):C- (NH₂).CS (X) and II.HCl or II.AcOH heated at 150-200° gave only X and tars. VI treated with P₂S₅ in pyridine, concentrated in vacuo, the residue decomposed with cold dilute aqueous NH₃, the mixture filtered, and the filtrate adjusted to pH 6 with AcOH gave only X, λ (pH 8.0) 249 and 344 mμ, R_f 0.33 (in A). IV (1 g.) and 2.5 g. Raney Ni in 50 ml. 5% aqueous NH₃ refluxed 70 min., filtered, the filtrate concentrated in vacuo, and kept overnight gave 150 mg. 8-methylpurine, λ (pH 8.0) 266 mμ, R_f 0.75 (in A).

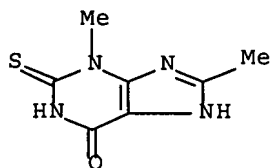
IT 91725-06-3P, Xanthine, 3,8-dimethyl-2-thio-

RL: PREP (Preparation)

(preparation of)

RN 91725-06-3 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,8-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 43 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1959:34829 CAPLUS Full-text

DOCUMENT NUMBER: 53:34829

ORIGINAL REFERENCE NO.: 53:6243f-i, 6244a-c

TITLE: Some new N-methylpurines

AUTHOR(S): Elion, Gertrude B.

CORPORATE SOURCE: Wellcome Research Labs., Tuckahoe, NY

SOURCE: Ciba Foundation Symposium, Chem. and Biol. Purines
(1957) 39-49

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

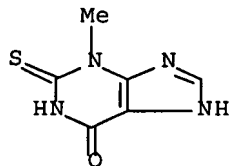
AB Ring closure in 5-formamido-4-amino-3-methyl-2-mercapto-6-oxopyrimidine (I) gave 2-mercapto-3-methylhypoxanthine (II), which on treatment with Raney Ni provided 3-methylhypoxanthine (III). I with Raney Ni gave 5-formamido-4-amino-3-methyl-6-oxopyrimidine which underwent ring closure with formamide to form III. III with P2S5 in pyridine provided 3-methyl-6-mercaptapurine which when treated with NH4OH at 140° for 16 h. gave 3-methyladenine (IV). Excellent yields of IV were obtained by treatment of II with P2S5 to form 3-methyl-2,6-dithiopurine, which was then converted to the 6-amino derivative and treated with Raney Ni to give IV. Methylation of 5-formamido-4-amino-2-mercapto-6-oxopyrimidine (V) with Me2SO4 in aqueous alkali gave the 2-methylthio-1-Me derivative (VI), as well as a water-soluble compound believed to be 4-amino-5-formamido-2-methylthio-6-methoxypyrimidine. VI with Raney Ni gave 5-formamido-4-amino-1-methyl-6-oxopyrimidine, which was converted to 1-methylhypoxanthine (VII) by heating with HCO2H. Treatment of VII with P2S5 in Tetralin or pyridine gave 1-methyl-6-mercaptapurine (VIII). Cyclization of VI with HCO2H gave 2-methylthio-1-methylhypoxanthine, which yielded 1-methylxanthine on acid hydrolysis and 1-methylguanine on heating with NH4OH. Heating of VIII with aqueous NH3 at 140° gave 4-amino-5-imidazolecarboxamide. With alc. NH3 at 160°, VIII was converted to 6-(methylamino)purine. VI with P2S5 in pyridine gave 2-methylthio-1-methyl-6-thiopurine, which when heated with NH4OH at 140° formed 1-methyl-2,6-diaminopurine. When 6-chloropurine was methylated and then treated with NaSH, 7-methyl- and 9-methyl-6-mercaptapurines were formed. These were easily separated because of a difference in solubility in water. 9-Methyladenine, prepared from 6-amino-2-methylthio-9-methylpurine, gave 9-methylhypoxanthine on treatment with HNO2. The UV absorption maximum (in mμ) at pH 1, 3, 7, and 11 were, for substituted hypoxanthines were (substituent given): H, 248, -, 249, 258; 1-Me, 249, -, 251, 260; 3-Me, 253, 262, 264, 265; 7-Me, 250, 255, 256, 262; 9-Me, 250, -, 250, 254. For substituted purines: 6-MeO, 254, -, 252, 261; 6-HS, 325, 323, 322, 233 (312); 1,6-Me(HS), 229(321), 233(321), 235(320), 237(321); 3,6-Me(HS), 244(334), 245(340), 245(337), 245(332); 7,6-Me(HS), 328, 328, 327, 234(315); 9,6-Me(HS), 323, 321, 320, 234(309); 6-MeS, 294, 290, 290, 290. At pH 1 and 11 for substituted adenines: H, 263, 267; 3-Me, 274, 273; 7-Me, 272, 271; 9-Me, 261, 262. 6-Methylaminopurine: 267, 272, at pH 1 and 11.

IT 28139-02-8P, Xanthine, 3-methyl-2-thio-

RL: PREP (Preparation)
(preparation of)

RN 28139-02-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-methyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1955:16071 CAPLUS Full-text

DOCUMENT NUMBER: 49:16071

ORIGINAL REFERENCE NO.: 49:3204a-i,3205a-c

TITLE: Syntheses in the purine series. III. Reactions of the acetates of 4,5-diaminouracil; the syntheses of caffeine, theobromine, and theophylline

AUTHOR(S): Brederick, Hellmut; Hennig, Ingeborg; Pfleiderer, Wolfgang; Weber, Gerhard

CORPORATE SOURCE: Tech. Hochschule, Stuttgart, Germany

SOURCE: Chemische Berichte (1953), 86, 333-51

CODEN: CHBEAM; ISSN: 0009-2940

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 49:16071

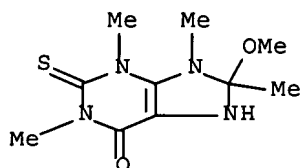
ED Entered STN: 22 Apr 2001

GI For diagram(s), see printed CA Issue.

AB IIIa (20 g.) was saponified 15 min. with 120 cc. 2N NaOH, and methylated 0.5 h. at 40° with 16 cc. Me₂SO₄ in 14 cc. Me₂CO giving, at 0° and pH 7.5. 90% [OC.NH.CO.NMe.C(NH₂):CNHAc.2H₂O (VI), m. 303° (from H₂O). IV could be isolated as an intermediate and subsequently methylated to VI. IIIa (10 g.) refluxed with 60 cc. 2N NaOH, decolorized, cooled to 40° and treated gradually with 19 cc. Me₂SO₄ and 12 cc. Me₂CO, maintaining pH 9 by dropwise addition of about 50 cc. 2N NaOH, over a 2-h. period. Subsequently the pH dropped to 7.5-8, and the mixture evaporated to 1/2 volume was kept 16 h. at 0° filtered from OC.NMe.CO.NMe.C(NH₂):C NHAc (VII) and extracted with CHCl₃ over a 30-h. period, the extraction being interrupted after 8 h., allowed to stand, filtered from precipitated VII, and the extraction continued with fresh CHCl₃. Total VII, 6-7 g., m. 281° (from CHCl₃. Methylating VI in KOH at 40° with EtOH and Me₂SO₄, yielded 80-90% VII. VI (10 g.) methylated in 2N NaOH at pH 9-10° the solution concentrated to 1/2 volume and extracted with CHCl₃ (as above), and the filtrates concentrated yielded 2 g. 4-Me derivative of VII, m. 247°. Further concentration of the CHCl₃ exts. gave a gummy residue yielding, when triturated with small amts. of Me₂CO, OC.NMe.CO.NMe.C(NHMe):CNMeAc, prisms, m. 225° (from EtOH). IIIa (5 g.) was converted into the Na salt of IIIb which, in 60 cc. H₂O was methylated 45 min. with 12 cc. Me₂SO₄ and 15 cc. Me₂CO, evaporated to 2/3 volume, and extracted 6 h. with CHCl₃ giving 1.5 g. OC.NMe.CO.NMe.C:C.NAc.CMe(OH).NH (VIII), m. 209° (from EtOH). IIIa (20 g.) saponified, and the product methylated with 105 cc. Me₂SO₄ at 40°, with the pH kept at 8-9 with 4N NaOH, concentrated to 1/2 volume and extracted 8 h. with CHCl₃ gave 10 g. OC.NMe.CO.NMe.C:C.NAc.CMe(OMe).NMe, m. 225° (from EtOH), also

formed in 60% yield from VIII by methylation at 40° and pH 7-8. VI (3 g.) refluxed 5 h. with 5 cc. Ac2O and 5 cc. pyridine yielded 2 g. 3,8-dimethylxanthine. VII (5.2 g.) refluxed 3-5 min. with 150 cc. Ac2O gave 4.8 g. OC.NMe.CO.NMe.C(NHAc):CNHAc (IX) (isomeric with VIII), hexagons, m. 235°, resolidifying at 250° to form 1,3,8-trimethylxanthine (X), m. 325°. By heating VII, IX, or VIII with Ac2O and pyridine, recrystg. the products from H2O and heating them above their m.ps. (about 215°) X was obtained, m. 325-30° (after sublimation). The 4-Me derivative of VII (1 g.) refluxed 6 h. with 20 cc. Ac2O and 10 cc. pyridine gave 8-acetoxy-1,3,8,9-tetramethyl-7-acetyl-1,2,3,6,8,9-hexahydropurine, m. 180° (from EtOH). I sulfate (2 g.) in EtCONH2 refluxed 20 min., followed by addition of 40 cc. EtOH gave 1.9 g. (crude) 4-amino-5-propionamidouracil (XI), having no characteristic m.p., 1 g. of which heated with HCONH2 gave 0.6 g. xanthine; the latter was also formed in high yield by heating either 5-formamido-4-aminouracil (XII) or IV in HCONH2. V (5 g.), brown powder, was formed by refluxing 10 g. I sulfate in 100 g. AcNH2. V was also prepared by refluxing XII, XI, or IV with AcNH2, and if any contaminating acyl derivs. were present, they were removed by refluxing with p-MeC6H4SO3H in MeOH. I sulfate (10 g.) refluxed 8 h. with EtCONH2, cooled to 60°, and extracted with MeOH gave 7 g. 8-ethylxanthine (XIII), which methylated at pH 8-9 and 40°, with Me2SO4 gave 8-ethylcaffeine, m. 184° (from EtOH). XIII was also formed by protracted heating of IV, XI, or XII in EtCONH2. Any adhering acyl derivs. were removed as above indicated. By refluxing VI 1 h. with 7.5 parts HCONH2, extracting with dilute NH4OH and precipitating with AcOH, 5 g. 3-methylxanthine (XIV) was obtained. XIV (10 g.) warmed at 100° with 80 cc. H2O and 35 cc. 2N NaOH, followed by methylating at pH 7-7.5 and 40° with 8.7 cc. Me2SO4 and 50 cc. MeOH, followed by direct crystallization at 0° and subsequent CHCl3 extraction gave 7-7.5 g. theophylline, m. 269° the latter was also formed by converting IIIa into crude VII and (without further purification) heating with HCONH2. The 4-Me derivative of VII (3 g.) refluxed 30 min. with 15 cc. HCONH2 gave 2 g. 1,3,8,9-tetramethylxanthine (XV), m. 254° (from EtOH), and, from the mother liquor from XV, after adding H2O and extracting with CHCl3 was obtained 1,3,9-trimethylxanthine (isocaffeine), m. 282-5° (from CHCl3, after trituration with Me2CO). XV was also formed by refluxing the 4-Me derivative of VII with AcNH2. VI (10 g.) refluxed 3 h. with MeOH containing 10-15% HCl gave the HCl salt of 4,5-diamino-3-methyluracil (XVI), yielding 6.2 g. of the free base with NH4OH. VII (10 g.) with MeOH-HCl as above gave the HCl salt of the 1-Me derivative of XVI, yielding 4.8 g. of the free base, m. 208-10°. VI (3 g.) refluxed 30 min. with 2N NaOH and acidified with 2N H2SO4 gave 2 g. 3,8-dimethylxanthine, needles, readily methylated to 1,3,7,8-tetramethylxanthine, m. 207-8° (from H2O). VII (3 g.) refluxed 1.5 h. with 60 cc. 0.3N NaOH and extracted with CHCl3 gave X, similarly obtained from VIII or IX. 8-Methoxy-2,6-dioxo-1,3,8,9-tetramethyl-7-acetyl-1,2,3,6,8,9-hexahydropurine (4 g.) refluxed 0.5 h. with 0.3N NaOH and extracted with CHCl3 gave the compound ClOH16O3N4, m. 246° (probably OC.NMe.CO.NMe.C:C.NH.CMe(OMe).NMe), the structure of which was not proved.

IT 841313-24-4P, Xanthine, 8,9-dihydro-8-methoxy-1,3,8,9-tetramethyl-
 RL: PREP (Preparation)
 (preparation of)
 RN 841313-24-4 CAPLUS
 CN Xanthine, 8,9-dihydro-8-methoxy-1,3,8,9-tetramethyl- (5CI) (CA INDEX
 NAME)



L9 ANSWER 45 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1951:61193 CAPLUS Full-text

DOCUMENT NUMBER: 45:61193

ORIGINAL REFERENCE NO.: 45:10401e-g

TITLE: Diuretic activity of compounds related to xanthines, uracils, and triazines as determined in dogs

AUTHOR(S): Kattus, Albert A.; Newman, Elliot V.; Franklin, John

CORPORATE SOURCE: Johns Hopkins Univ., Baltimore, MD

SOURCE: Bulletin of the Johns Hopkins Hospital (1951), 89, 1-8
CODEN: JHHBAI; ISSN: 0097-1383

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

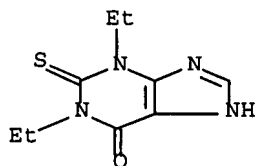
ED Entered STN: 22 Apr 2001

AB A series of 19 substituted xanthines, 1 thioxanthine, 14 uracils, 1 thiouracil, 3 triazines, 2 phenothiazines, and a substituted N-benzylaniline were tested for diuretic activity in female dogs. Urine vols. and Na excretions from dogs receiving two 0.25-0.5-g. doses in 1 day were compared with those from the same dogs prior to dosing. With Na excretion as a criterion, 1,3-diethylxanthine (I), its 2-thio analog, and its 8-bromo derivative (II) were highly diuretic, but caused emesis. Emesis was also noted with other 1,3-dialkylxanthines. In human subjects I caused diuresis and vomiting, but II had neither action. Except for 1-propyl-3-ethyl-6-aminouracil, uracil derivs. were less active than the xanthine derivs. and produced less gastrointestinal disturbance; 2,4-bis(acetamido)-s-triazine produced diuresis in a human volunteer.

IT 841313-23-3, Xanthine, 1,3-diethyl-2-thio-
(diuretic activity of)

RN 841313-23-3 CAPLUS

CN Xanthine, 1,3-diethyl-2-thio- (5CI) (CA INDEX NAME)



L9 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1931:52428 CAPLUS Full-text

DOCUMENT NUMBER: 25:52428

ORIGINAL REFERENCE NO.: 25:5894f-i

TITLE: Methylcaffeidine

AUTHOR(S): Biltz, Heinrich; Rakett, Hans

SOURCE: Berichte der Deutschen Chemischen Gesellschaft
[Abteilung] B: Abhandlungen (1931), 64B, 1970-4
CODEN: BDCBAD; ISSN: 0365-9488

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 16 Dec 2001

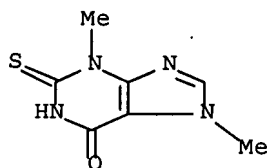
GI For diagram(s), see printed CA Issue.

AB Some yrs. ago it was briefly (C. A. 22, 4477) reported that caffeidine (I) can be methylated with Me₂SO₄ to methylcaffeidine (II), which was characterized as a perchlorate m. 173°. Often, however, the II so obtained was not pure and further study has shown that the action of Me₂SO₄ on I is very slow and may easily lead to the formation of mixts. of I and II. Recourse was therefore again had to MeI, which gives an equimol. mixture of II and I.HI, readily separated by means of CHCl₃. In this way pure II, m. 98-9°, is obtained in 1.6 g. yield from 3.4 g. I. the I.HI (2.6 g.) m. 247-9°, solubility about 4.4 in boiling alc. and 1.1 at room temperature Salts of II: perchlorate, m. 173°; chloroaurate, lemon-yellow, very unstable; Ag nitrate, [Ag(C₈H₁₄ON₄)]NO₃, easily decomposed by light or by organic compds. and non-noble metals, can often, with care, be crystallized from water. Salts of I: chloroplatinate, orange; chloroaurate, wine- to brown-red, deposits Au on attempted crystallization from water; fluoborate, m. 219° (decomposition); thiocyanate, m. 197°, yields on heating 2 hrs. at 160-70° a small quantity (0.12 g. from 2 g. of the salt) of what is apparently 2-thiotheobromine, m. 298°, solubility in boiling water about 0.3. II gently warmed with MeI gives a HI salt, C₉H₁₈O₂N₄.HI, m. 153° (decomposition), which reacts with AgNO₃ in water. II therefore has the structure N:CH.NMe.C(CONHMe:CNMe₂. I fused with MeNHCONH₂ or EtNHCONH₂ yields theobromine; in both cases the alkylurea gives HOCN, which adds to the NHMe residue of the I (position 3 of the purine nucleus) and forms a ring by displacing the other NHMe group (position 1). Similarly, fusion with CO(NHMe)₂ gives caffeine, with CO(NHEt)₂ 1-ethyltheobromine. With PhNHCONH₂ and CO(NHPh)₂ there is no reaction.

IT 19373-97-8P, Theobromine, 2-thio-
RL: PREP (Preparation)
(preparation of)

RN 19373-97-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3,7-dimethyl-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 47 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1928:37616 CAPLUS Full-text

DOCUMENT NUMBER: 22:37616

ORIGINAL REFERENCE NO.: 22:4477c-i,4478a-e

TITLE: Caffeidine and caffeidinecarboxylic acid

AUTHOR(S): Biltz, Heinrich; Rakett, Hans

CORPORATE SOURCE: Univ. Breslau

SOURCE: Berichte der Deutschen Chemischen Gesellschaft
[Abteilung] B: Abhandlungen (1928), 61B, 1409-22

DOCUMENT TYPE:

Journal

LANGUAGE:

Unavailable

ED Entered STN: 16 Dec 2001

GI For diagram(s), see printed CA Issue.

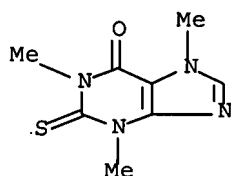
AB Caffeine with alkalies takes up 1 mol. H₂O to form caffeidinecarboxylic acid (I), which by loss of CO₂ gives caffeidine; this, from its monobasic character and its reactions must have the structure II. Whether in the formation of I the purine ring is broken between positions 1 and 2 or 2 and 3 was not known but the present work shows that it is between 1 and 2 and hence that I has the structure III. In its preparation 2 N NaOH in moderate excess was used instead of Ba(OH)₂ and heating was avoided; by shaking with a machine, the time necessary for the reaction was reduced from more than 2 weeks to 3-4 days. From the cooked solution the II can be precipitated directly with HNO₃ as the difficultly soluble nitrate (hitherto described as a hygroscopic substance), and from the mother liquors that I is obtained as the Cu salt by the original May and Andreasch method. II behaves as a monoacid base (with HCl, HI, HNO₃, HClO₄, H₂PtCl₆). With H₂SO₄ it forms a 1:1 salt, to be sure, but this is undoubtedly an acid salt. Since caffeine is monoacid through the 9-N atom and the imidazole ring of II is the same as that in caffeine, the basic nature of II is probably due to the same N atom (3 in the notation for II). The MeNH group on C atom 4 is apparently not capable of adding acids, probably because of the adjacent 4,5-double bond. In agreement with this view is the fact that I, whose 8-N atom certainly does not add acids, forms with acids salts like caffeine and II. II also forms a complex Ag salt [Ag(C₇H₁₂ON₄)₂NO₃] with AgNO₃. The action of HNO₂ on II shows that the 8-N atom is secondary. The 7-MeNH group does not react with HNO₂, for allo-caffuric acid can in no way be nitrosated. Since I does not react with HNO₂, the CO₂H group must be on N atom 8, as shown in formula III. Similarly II can and I cannot be benzoylated. The 1st Me group which can be introduced with MeI certainly enters the same position; the 2nd Me group, which can be likewise introduced with MeI, may enter position 7 but this is not proved. Me₂SO₄ introduces only one Me group. The smooth transformation of II into 1,3-dimethylparabanic acid does not seem to harmonize with the structure given for II; it would appear to indicate that II contains a ring with two NMe groups. The explanation is doubtless that the reaction is complicated; the II splits open between positions 2 and 3, a CO₂H group is produced at 2, and this with the NHMe group at 8 forms the new ring of the parabanic acid, the N atoms at 3 and 7 being split off by oxidation at the same time. The presence of the 4,5-double bond in II can be shown by means of Cl in MeOH and H₂O; in MeOH is obtained caffeidine-4,5-glycol di-Me ether (IV), while with Cl water the II likewise adds two HO groups at the double bond but at the same time oxidation occurs at 2 and the MeNHCO group at 6 is split off, the product being 1-methyl-2-heto-1-methylaminotetrahydroimidazole-4,5-glycol (V) II can be converted back to caffeine, with 50% yield, with ClCO₂Et or KOCN, and, through the amide of I, into theobromine. With CSCl₂ is obtained a 2-thiocaffeine (VI), which can be converted in CHCl₃ into the 8-Cl derivative (VII), and this with NaOMe gives the 8-MeO compound (VIII), which can be rearranged into 2-thiotetramethyluric acid (IX) or converted with HCl into 1,3,7-trimethyl-2-thiouric acid (X). Finally VII was converted into 1,3,7-trimethyl-2,8-dithiouric acid (XI) and, by alkylation, into various ethers of 2-thio-8-thiocaffeine (XII). Nitrate of II (yield, 41%), m. 215° (decomposition), solubility in boiling H₂O about 50, H₂O at room temperature about 2, boiling MeOH about 2.7, boiling AcOH about 15 (with decomposition). II, as determined by J. Pohl, has no diuretic action and does not affect the blood pressure. Perchlorate, m. 220-1° (decomposition), solubility in boiling MeOH and EtOH about 8.6; HCl salt, m. 215° (decompose), is not deliquescent when pure. Bz derivative, m. 174°, decomposed by alkalies, stable towards dilute acids, forms no salts with acids. NO derivative, m. 155° (effervescence), quite stable towards even concentrated NaOH at room temperature, forms no salts with

acids. Methylcaffeidine (3.5 g. from 5 g. II.HNO₃ and alkaline Me₂SO₄), m. 86° perchlorate, m. 173°, solubility in MeOH at room temperature 1.8, at the b. p. about 8. IV.HCl (2.5 g. from 5 g. II in cold dry alc. with Cl); free IV, m. 164°. V.HCl, crystals with 1 H₂O, m. 112°, belonging (according to J. Valetton) to the monoclinic holohedral class, β 116° 17', a:b:c = 1.074:1:1.480, gives (CO₂H)₂ when dissolved in boiling 2 N NaOH and then boiled a short time with AcOH. Free V, prepared from the HCl salt with KOCN (but not with NaOH, Na₂CO₃, Ba(OH)₂, PbCO₃ or Ag₂O), m. 163° (effervescence), solubility in alc. at room temperature about 0.3, at the b. p. 1. Amide of I, from II and urea with HCl gas at 135-40°, m. 244-5°, gives theobromine on long boiling in mineral acids or AcOH, evaporation with concentrated HCl, boiling with Na₂CO₃ and acidifying with AcOH, treating with HCl gas in alc. or heating above its m. p. VI (20-2 g. from 25 g. JJ II. HNO₃), light yellow, sinters 203°, m. 205°, soluble in concentrated mineral acids but repptd. on dilution, much more bitter than caffeine and has a strong diuretic action; perchlorate, deflagrates on Pt, m. 239-40° (decomposition), hydrolyzed by boiling H₂O or alc. VII (6-7 g. from 8.6 g. VI), yellow, m. 186-7°, easily soluble in concentrated acids. VIII (1.5-1.7 g. from 2 g. VII), m. 174°, solubility in boiling alc. about 25. IX, from VIII in MeOH at 200°, darkens 260°, m. 297-8°. X, m. 343°, apparently with decomposition, soluble in alkalies and concentrated mineral acids. XI (2.5 g. from 3 g. VII with boiling aqueous KSH), yellow, m. 285°, solubility in boiling H₂O about 0.8, easily soluble in alkalies and repptd. by acids; Na and K salts, yellow. Me ether of XII (0.8 g. from 1 g. XI with alkaline Me₂SO₄), m. 183°, solubility in alc. about 5. Et ether (0.9 g. from 1 g. XI with EtBr and KOH), light yellow, m. 156°. Allyl ether, yellow, m. 98°. I m. 159° (decomposition); AcOH compound, m. 127-9°; nitrate, m. 173° (effervescence); perchlorate, m. 167-8° (effervescence); HCl salt, m. 179° (decomposition).

IT 24049-32-9P, Caffeine, 2-thio- 879683-47-3P, Caffeine,
2-thio-, perchlorate
RL: PREP (Preparation)
(preparation of)

RN 24049-32-9 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-1,3,7-trimethyl-2-thioxo- (9CI) (CA INDEX NAME)



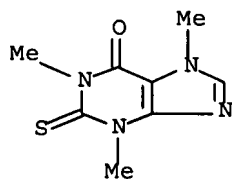
RN 879683-47-3 CAPLUS

CN Caffeine, 2-thio-, perchlorate (3CI) (CA INDEX NAME)

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CRN 24049-32-9

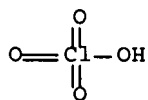
CMF C8 H10 N4 O S



CM 2

CRN 7601-90-3

CMF Cl H O4



Search History

L1 STRUCTURE UPLOADED
L2 0 SEA SSS SAM L1
L3 21 SEA SSS FUL L1

FILE 'CAPLUS' ENTERED AT 14:21:09 ON 13 APR 2007

L4 48 SEA ABB=ON PLU=ON L3
L5 378 SEA ABB=ON PLU=ON HANSON S?/AU
L6 0 SEA ABB=ON PLU=ON NORDVAL G?/AU
L7 17 SEA ABB=ON PLU=ON TIDEN A?/AU
L8 1 SEA ABB=ON PLU=ON (L5 OR L6) AND L7

L9 47 SEA ABB=ON PLU=ON L4 NOT L8

=>

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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: MARK BERTH Examiner #: 59193 Date: 4/13/02
 Art Unit: 1624 Phone Number: 2- 0663 Serial Number: 10511537 A
 Location (Bldg/Room#): 5C01 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following: ME

Title of Invention: _____

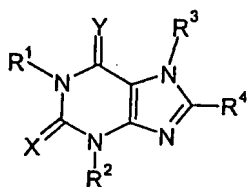
Inventors (please provide full names): _____

Earliest Priority Date: _____

Search Topic:

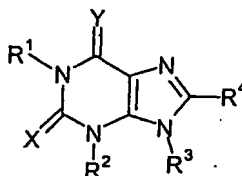
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



(Ia)

or



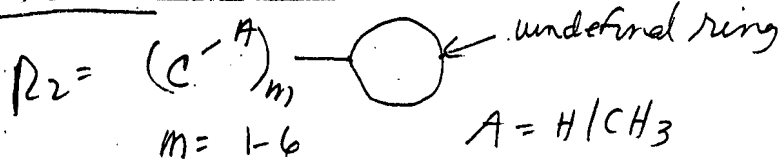
(Ib)

wherein:

X represents S, and Y represents C;

R1 represents hydrogen or C1 to 6 alkyl;

R2, R3, R4,



20070412-10511537-otr1

STAFF USE ONLY

Searcher: POB

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 4-12-07Searcher Prep & Review Time: 20Online Time: 11

Type of Search

____ NA Sequence (#)

____ AA Sequence (#)

3 Structure (#)

____ Bibliographic

____ Litigation

____ Fulltext

____ Other

Vendors and cost where applicable

065 STN _____ Dialog

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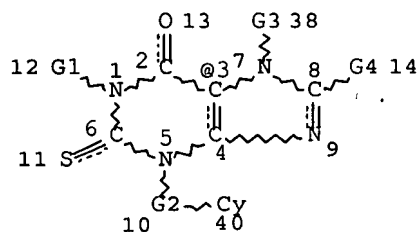
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Search #2 Claim 8 & some claim 9 species

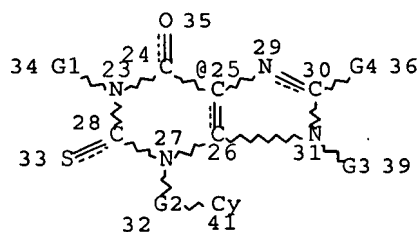
STEREO ATTRIBUTES: NONE

L4 17287 SEA FILE=REGISTRY SSS FUL L1

L5 STR



Ak @15



G10 37

VAR G1=H/15

REP G2=(1-6) C

VAR G3=H/15

VAR G4=H/15

VAR G10=3/25

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 15

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE

L8 17 SEA FILE=REGISTRY SUB=L4 SSS FUL L5

100.0% PROCESSED 229 ITERATIONS

17 ANSWERS

SEARCH TIME: 00.00.01

=> fil capl; s l8

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FILE LAST UPDATED: 11 Apr 2007 (20070411/ED)

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L9 8 L8

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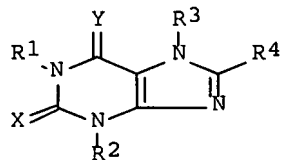
L9 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:855927 CAPLUS Full-text
 DOCUMENT NUMBER: 139:350580
 TITLE: Preparation of xanthinethione derivatives as
 myeloperoxidase inhibitors
 INVENTOR(S): Hanson, Sverker; Nordvall, Gunnar; Tiden, Anna-Karin
 PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
 SOURCE: PCT Int. Appl., 55 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003089430 | A1 | 20031030 | WO 2003-SE617 | 20030415 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2480452 | A1 | 20031030 | CA 2003-2480452 | 20030415 |
| AU 2003224548 | A1 | 20031103 | AU 2003-224548 | 20030415 |
| EP 1499613 | A1 | 20050126 | EP 2003-721211 | 20030415 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003009012 | A | 20050201 | BR 2003-9012 | 20030415 |
| CN 1646531 | A | 20050727 | CN 2003-808355 | 20030415 |
| JP 2005526836 | T | 20050908 | JP 2003-586151 | 20030415 |
| NZ 535406 | A | 20060831 | NZ 2003-535406 | 20030415 |
| ZA 2004007815 | A | 20051004 | ZA 2004-7815 | 20040928 |
| US 2005234036 | A1 | 20051020 | US 2004-511537 | 20041015 |
| NO 2004004998 | A | 20050118 | NO 2004-4998 | 20041117 |
| PRIORITY APPLN. INFO.: | | | SE 2002-1193 | A 20020419 |
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| | | | WO 2003-SE617 | W 20030415 |

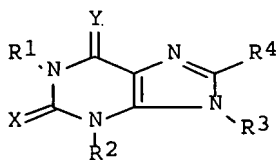
OTHER SOURCE(S): MARPAT 139:350580

ED Entered STN: 31 Oct 2003

GI



I



II

AB Xanthinethiones I and II [one of X and Y = S, the other = O, S; R1, R3, R4 = H, alkyl; R2 = H, (un)substituted alkyl] were prepared for use as myeloperoxidase (MPO) inhibitors in the treatment of neuroinflammatory disorders. Thus, Me2CHCH2NHCSNH2 was cyclized with NCCH2CO2Et to give 6-amino-1-isobutyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one which was nitrosated, reduced to the 5,6-diamine, and cyclized with HCO2H to give II [R1, R3, R4 = H, R2 = CH2CHMe2, X = S, Y = O]. This compound had IC50 for inhibition of MPO of 0.87 μ M.

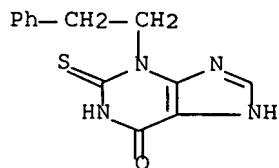
IT 139460-82-5P 618913-20-5P 618913-24-9P
618913-26-1P 618913-27-2P 618913-28-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

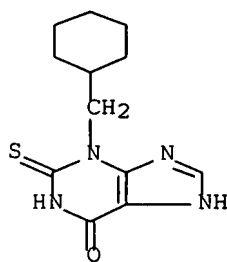
RN 139460-82-5 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(2-phenylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



RN 618913-20-5 CAPLUS

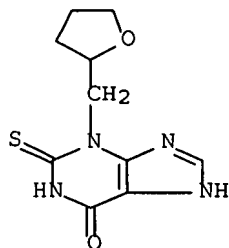
CN 6H-Purin-6-one, 3-(cyclohexylmethyl)-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



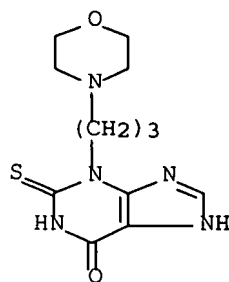
RN 618913-24-9 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[(tetrahydro-2-furanyl)methyl]-2-

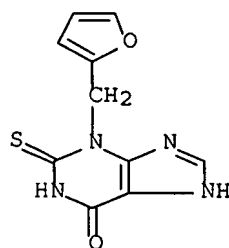
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RN 618913-26-1 CAPLUS

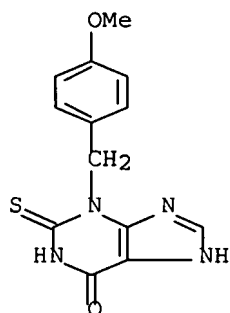
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-2-thioxo-
(9CI) (CA INDEX NAME)

RN 618913-27-2 CAPLUS

CN 6H-Purin-6-one, 3-(2-furanylmethyl)-1,2,3,7-tetrahydro-2-thioxo- (9CI)
(CA INDEX NAME)

RN 618913-28-3 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[(4-methoxyphenyl)methyl]-2-thioxo-
(9CI) (CA INDEX NAME)



IT 618913-30-7P 618913-31-8P

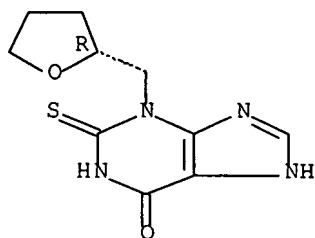
RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

RN 618913-30-7 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[[4-methoxyphenyl]methyl]-2-thioxo- (9CI) (CA INDEX NAME)

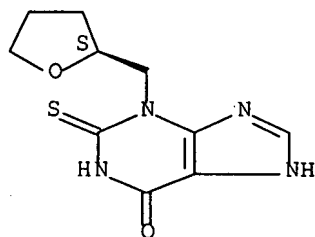
Absolute stereochemistry.



RN 618913-31-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[[2S]-tetrahydro-2-furanyl]methyl]-2-thioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 618913-22-7P 618913-29-4P

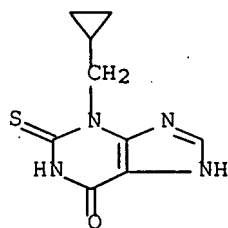
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of xanthinethione derivs. as myeloperoxidase inhibitors)

RN 618913-22-7 CAPLUS

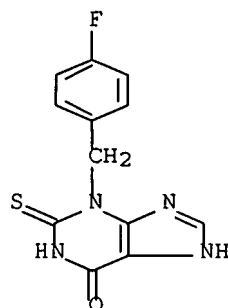
Search #2 Claim 8 & some claim 9 species

CN 6H-Purin-6-one, 3-(cyclopropylmethyl)-1,2,3,7-tetrahydro-2-thioxo- (9CI)
(CA INDEX NAME)



RN 618913-29-4 CAPLUS

CN 6H-Purin-6-one, 3-[(4-fluorophenyl)methyl]-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:502824 CAPLUS Full-text

DOCUMENT NUMBER: 137:63122

TITLE: Preparation of purine derivatives or therapeutic use as phosphodiesterase IV inhibitors

INVENTOR(S): Chasin, Mark; Cavalla, David J.; Hofer, Peter; Gehrig, Andre; Wintergerst, Peter

PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg

SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 285,473.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 21

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 6413975 | B1 | 20020702 | US 2000-539571 | 20000331 |
| IN 180930 | A1 | 19980404 | IN 1995-CA1508 | 19951123 |
| IN 181538 | A1 | 19980711 | IN 1995-CA1506 | 19951123 |
| HU 200200938 | A2 | 20021028 | HU 2002-938 | 20000331 |
| JP 2001316314 | A | 20011113 | JP 2000-136383 | 20000509 |

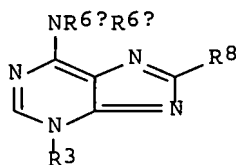
Search #2 Claim 8 & some claim 9 species

US 2003073834
PRIORITY APPLN. INFO.:

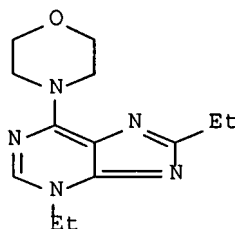
A1 20030417

| | |
|----------------|-------------|
| US 2002-62280 | 20020201 |
| US 1999-285473 | A2 19990402 |
| IN 1994-CA514 | A1 19940630 |
| US 1997-963054 | A2 19971103 |
| US 1997-875487 | A2 19971113 |
| US 1998-151949 | A2 19980911 |
| US 1998-210556 | A2 19981211 |
| US 1998-210557 | A2 19981211 |
| US 1999-227057 | A2 19990107 |
| US 1999-237638 | A2 19990126 |
| US 1999-361196 | A2 19990726 |
| US 2000-506624 | A2 20000218 |
| US 2000-539571 | A2 20000331 |
| US 2000-547575 | A2 20000412 |
| US 2000-547898 | A2 20000412 |
| US 2000-636146 | A2 20000810 |
| US 2000-724321 | B1 20001128 |

OTHER SOURCE(S): MARPAT 137:63122
ED Entered STN: 04 Jul 2002
GI



I



II

AB Purines, such as I [R3, R6a, R6b, R8 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, etc.], were prepared for pharmaceutical use as phosphodiesterase IV (PDE IV) inhibitors. Thus, 3,8-diethyl-6-morpholino- 3H-purine (II) was prepared by conversion of 3,8-diethyl-2-thioxanthine to 3,8-diethylhypoxanthine using 2N NaOH and nickel aluminum alloy, reaction of 3,8-diethylhypoxanthine to 3,8-diethyl-6-thiohypoxanthine using phosphorus pentasulfide in pyridine and, finally, reaction of 3,8-diethyl-6-thiohypoxanthine with morpholine. The prepared purine derivs. were assayed for PDE IV inhibition.

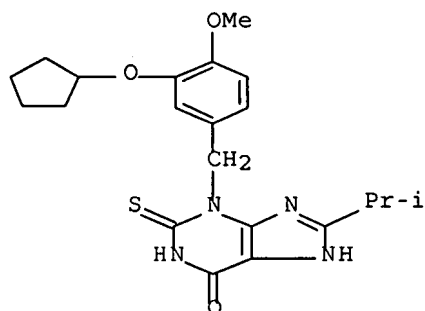
IT 300781-30-0P, 3-(3-Cyclopentyloxy-4-methoxybenzyl)-8-isopropyl-2-thioxanthine 300781-35-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of purine derivs. for therapeutic use as phosphodiesterase IV inhibitors)

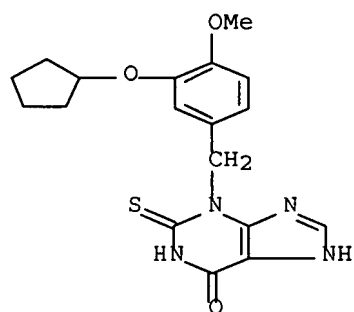
RN 300781-30-0 CAPLUS

CN 6H-Purin-6-one, 3-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-1,2,3,7-tetrahydro-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



RN 300781-35-5 CAPLUS

CN 6H-Purin-6-one, 3-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:136945 CAPLUS Full-text

DOCUMENT NUMBER: 134:193441

TITLE: Preparation of hypoxanthines and thiohypoxanthines as phosphodiesterase IV inhibitors

INVENTOR(S): Chasin, Mark; Hofer, Peter; Cavalla, David

PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

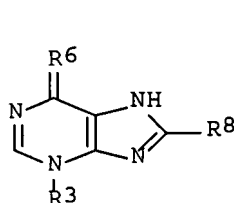
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2001011967 | A1 | 20010222 | WO 2000-US21836 | 20000809 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, | | | | |

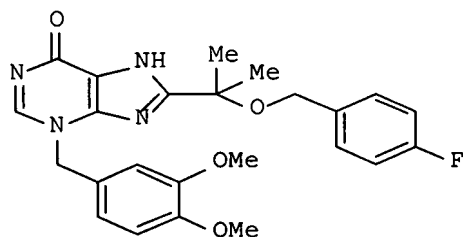
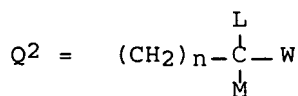
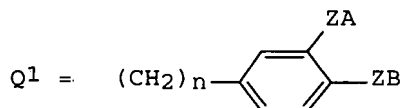
Search #2 Claim 8 & some claim 9 species

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|--|----|----------|-----------------|------------|
| CA 2379356 | A1 | 20010222 | CA 2000-2379356 | 20000809 |
| EP 1202628 | A1 | 20020508 | EP 2000-953925 | 20000809 |
| EP 1202628 | B1 | 20041013 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003506467 | T | 20030218 | JP 2001-516330 | 20000809 |
| AT 279113 | T | 20041015 | AT 2000-953925 | 20000809 |
| PRIORITY APPLN. INFO.: | | | US 1999-148623P | P 19990812 |
| | | | WO 2000-US21836 | W 20000809 |
| OTHER SOURCE(S): MARPAT 134:193441 | | | | |
| ED Entered STN: 25 Feb 2001 | | | | |
| GI | | | | |



I

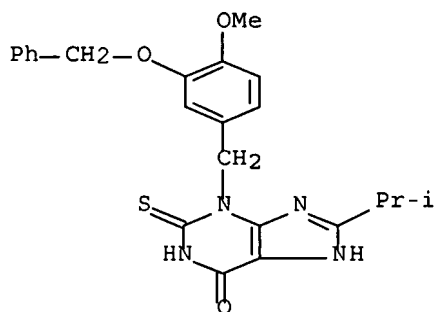


II

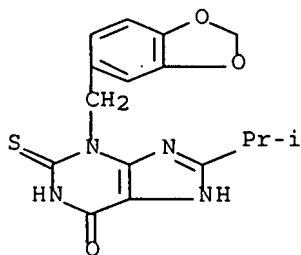
AB Title compds. (I) [wherein R3 and R8 = independently (cyclo)alkyl, alkenyl, alkynyl, Q1, or Q2; R6 = S or O; n = 0-1; Z = a bond, CH2, NH, O, or S; A and B can form a ring by adding 1-3 CH2 groups when Z = CH2, NH, O or S; and A and B are not in a ring when Z = a bond, wherein A and B = independently H, halo, (cyclo)alkyl, (cyclo)alkoxy, OH, or (un)substituted Ph, benzyl, or benzyloxy; L and M = independently H or Me; W = Q1, OH, (hetero)aryl, heterocyclyl, or (un)substituted benzyloxy] were prepared as selective phosphodiesterase (PDE) IV inhibitors. For example, amidation of 2-(4-fluorobenzyl)-2-methylpropionyl chloride with 5,6-diamino-1-(3,4-dimethoxybenzyl)-2-thiouracil using TEA in THF (20.4%), followed by cyclization with NaOH to form the 2-thioxanthine (79.1%) and treatment with Raney nickel in 1-propanol (67.2%), afforded the hypoxanthine (II). In assays measuring isolated PDE isoenzyme activity, II selectively inhibited PDE IV compared to PDE III and PDE V with IC50 values of 1.079 μM , 69.62 μM , and 35.80 μM , resp. As a result, I are expected to induce the desirable anti-asthmatic effects associated with PDE IV inhibition without causing the undesirable cardiovascular stimulation associated with PDE III inhibition (no data). I are useful in the treatment of asthma, allergies, inflammation, depression, dementia, and other disease states associated with abnormally high physiolog. levels of cytokine (no data).

Search #2 Claim 8 & some claim 9 species

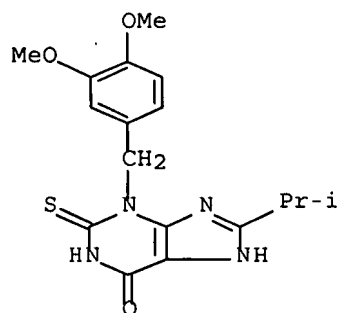
IT 227763-83-9P, 3-(3-Benzoyloxy-4-methoxybenzyl)-8-isopropyl-2-thioxanthine 327036-65-7P, 3-(3,4-Methylenedioxybenzyl)-8-(1-methylethyl)-2-thioxanthine 327036-70-4P, 3-(3,4-Dimethoxybenzyl)-8-(1-methylethyl)-2-thioxanthine
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of hypoxanthine and thiohypoxanthine phosphodiesterase IV inhibitors from thiouracils and acyl halides and anhydrides)
 RN 227763-83-9 CAPLUS
 CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[[4-methoxy-3-(phenylmethoxy)phenyl]methyl]-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



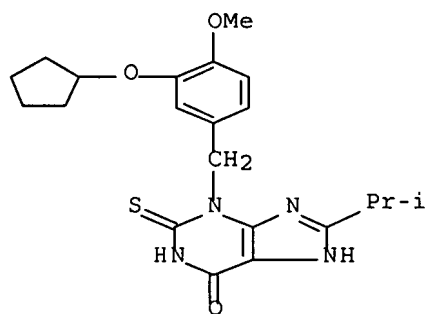
RN 327036-65-7 CAPLUS
 CN 6H-Purin-6-one, 3-(1,3-benzodioxol-5-ylmethyl)-1,2,3,7-tetrahydro-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



RN 327036-70-4 CAPLUS
 CN 6H-Purin-6-one, 3-[(3,4-dimethoxyphenyl)methyl]-1,2,3,7-tetrahydro-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



IT 300781-30-0, 3-(3-Cyclopentyloxy-4-methoxybenzyl)-8-isopropyl-2-thioxanthine
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (starting material; preparation of hypoxanthine and thiohypoxanthine phosphodiesterase IV inhibitors from thiouracils and acyl halides and anhydrides)
 RN 300781-30-0 CAPLUS
 CN 6H-Purin-6-one, 3-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-1,2,3,7-tetrahydro-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:725418 CAPLUS Full-text
 DOCUMENT NUMBER: 133:296324
 TITLE: Synthesis and phosphodiesterase IV inhibition activity of purine derivatives
 INVENTOR(S): Chasin, Mark; Cavalla, David; Hofer, Peter; Gehrig, Andre; Wintergest, Peter
 PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
 SOURCE: PCT Int. Appl., 112 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 21
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2000059449 | A2 | 20001012 | WO 2000-US8525 | 20000331 |

Search #2 Claim 8 & some claim 9 species

WO 2000059449 A3 20010104

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|------------|----|----------|-----------------|----------|
| IN 180930 | A1 | 19980404 | IN 1995-CA1508 | 19951123 |
| IN 181538 | A1 | 19980711 | IN 1995-CA1506 | 19951123 |
| CA 2367143 | A1 | 20001012 | CA 2000-2367143 | 20000331 |
| EP 1169321 | A2 | 20020109 | EP 2000-919929 | 20000331 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

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|---------------|----|----------|----------------|----------|
| HU 200200938 | A2 | 20021028 | HU 2002-938 | 20000331 |
| JP 2002541078 | T | 20021203 | JP 2000-609014 | 20000331 |
| BR 2000011182 | A | 20030610 | BR 2000-11182 | 20000331 |
| JP 2001316314 | A | 20011113 | JP 2000-136383 | 20000509 |

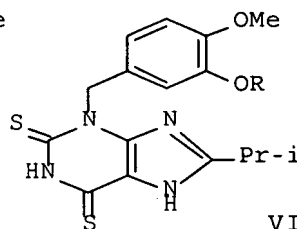
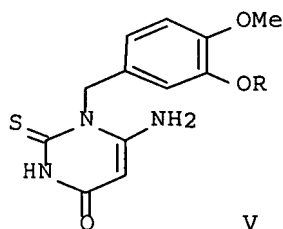
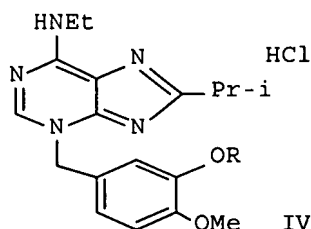
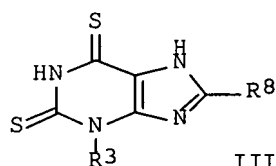
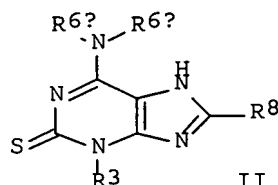
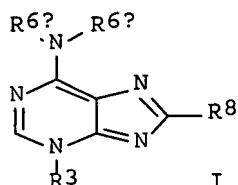
PRIORITY APPLN. INFO.:

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| US 1999-285473 | A | 19990402 |
| IN 1994-CA514 | A1 | 19940630 |
| WO 2000-US8525 | W | 20000331 |

OTHER SOURCE(S): MARPAT 133:296324

ED Entered STN: 13 Oct 2000

GI



AB The purine (I) (R3, R8, R6a, R6b = H, (un)substituted alkyl, alkenyl, cycloalkyl, aryl, heterocyclyl, heteroaryl etc.), thioisoguanine (II), dithioxanthine (III) derivs., and their pharmaceutically accepted salts were synthesized. Thus, purine (IV; R = (CH₂)₅) was prepared by etherification of isovanilline with cyclopentanol, oximation, reduction to amine, conversion to isothiocyanate, amination to thiourea followed by heterocyclization with Et cyanoacetate to thiouracil (V). V was nitrosylated, reduced, reacted with isobutyric anhydride to give isobutyrylamine which on treatment with phosphorus pentasulfide gave dithioxanthine (VI). VI, in a pressure reactor gave purine-2-thione which was reduced with Raney-nickel to give IV. The IC₅₀

Search #2 Claim 8 & some claim 9 species

of IV against phosphodiesterase IV inhibition was 0.32 μ M. I, II and III were effective in effecting PDE IV inhibition in patients in need thereof.

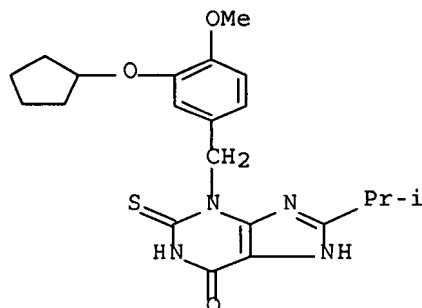
IT 300781-30-0P 300781-35-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of purine derivs. as phosphodiesterase IV inhibitors)

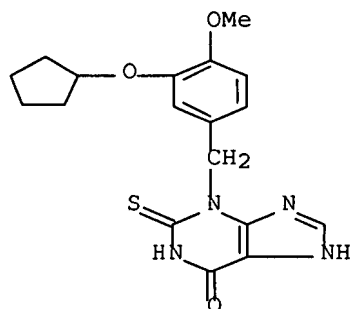
RN 300781-30-0 CAPLUS

CN 6H-Purin-6-one, 3-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-1,2,3,7-tetrahydro-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



RN 300781-35-5 CAPLUS

CN 6H-Purin-6-one, 3-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-1,2,3,7-tetrahydro-2-thioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:404966 CAPLUS Full-text

DOCUMENT NUMBER: 131:58700

TITLE: Preparation of purine derivatives having phosphodiesterase IV inhibiting activity

INVENTOR(S): Cavalla, David; Chasin, Mark; Hofer, Peter; Gehrig, Andre; Wintergerst, Peter

PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 21

PATENT INFORMATION:

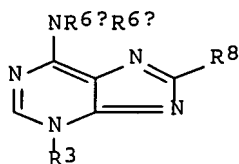
Search #2 Claim 8 & some claim 9 species

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|-------------|
| WO 9931102 | A1 | 19990624 | WO 1998-US26293 | 19981211 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| IN 180930 | A1 | 19980404 | IN 1995-CA1508 | 19951123 |
| IN 181538 | A1 | 19980711 | IN 1995-CA1506 | 19951123 |
| US 6037470 | A | 20000314 | US 1998-209658 | 19981210 |
| US 6040447 | A | 20000321 | US 1998-209922 | 19981210 |
| US 6057445 | A | 20000502 | US 1998-209664 | 19981210 |
| CA 2314335 | A1 | 19990624 | CA 1998-2314335 | 19981211 |
| AU 9918159 | A | 19990705 | AU 1999-18159 | 19981211 |
| AU 747366 | B2 | 20020516 | | |
| BR 9815171 | A | 20001010 | BR 1998-15171 | 19981211 |
| EP 1045849 | A1 | 20001025 | EP 1998-963053 | 19981211 |
| EP 1045849 | B1 | 20030702 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| TR 200001706 | T2 | 20001121 | TR 2000-200001706 | 19981211 |
| US 6211367 | B1 | 20010403 | US 1998-210557 | 19981211 |
| US 6228859 | B1 | 20010508 | US 1998-210556 | 19981211 |
| HU 200100417 | A2 | 20011228 | HU 2001-417 | 19981211 |
| HU 200100417 | A3 | 20020429 | | |
| JP 2002508376 | T | 20020319 | JP 2000-539025 | 19981211 |
| JP 3504234 | B2 | 20040308 | | |
| AT 244243 | T | 20030715 | AT 1998-963053 | 19981211 |
| PT 1045849 | T | 20031128 | PT 1998-963053 | 19981211 |
| ES 2202924 | T3 | 20040401 | ES 1998-963053 | 19981211 |
| NO 2000002998 | A | 20000719 | NO 2000-2998 | 20000609 |
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| | | | IN 1994-CA514 | A1 19940630 |
| | | | WO 1998-US26293 | W 19981211 |

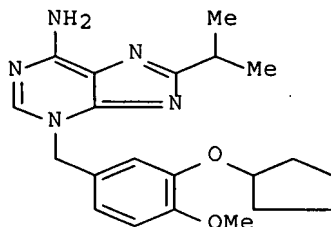
OTHER SOURCE(S): MARPAT 131:58700

ED Entered STN: 01 Jul 1999

GI



I



II

AB Purines I [R₃ = alkyl, alkenyl, cycloalkyl, cycloalkenyl, wherein said alkyl, alkenyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl; R_{6a}, R_{6b} = H, alkyl, alkenyl, cycloalkyl, cycloalkenyl; R₈ = H, alkyl, alkenyl, cycloalkyl,

Search #2 Claim 8 & some claim 9 species

cycloalkenyl] were prepared for use as phosphodiesterase inhibitors for the treatment of diseases such as asthma, allergy, or inflammation. Thus, purine derivative II was prepared starting from 3-(3-cyclopentyloxy-4-methoxybenzyl)-8-isopropylhypoxanthine. The prepared purines were tested for inhibitory activity against phosphodiesterase types III, IV, and V.

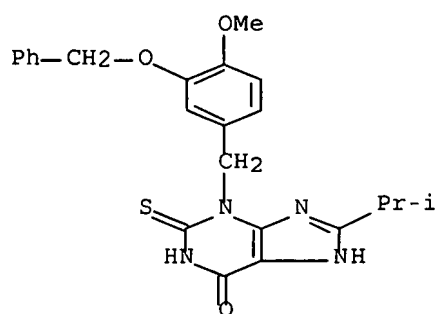
IT 227763-83-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of purine derivs. having phosphodiesterase IV inhibition activity)

RN 227763-83-9 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-[[4-methoxy-3-(phenylmethoxy)phenyl]methyl]-8-(1-methylethyl)-2-thioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:214213 CAPLUS Full-text

DOCUMENT NUMBER: 116:214213

TITLE: Inhibitors of human purine nucleoside phosphorylase. Synthesis and biological activities of

8-amino-3-benzylhypoxanthine and related analogs

AUTHOR(S): Woo, Peter W. K.; Kostlan, Catherine R.; Sircar, Jagadish C.; Dong, Mi K.; Gilbertsen, Richard B.

CORPORATE SOURCE: Parke-Davis Pharm. Res. Div., Warner-Lambert Co., Ann Arbor, MI, 48105, USA

SOURCE: Journal of Medicinal Chemistry (1992), 35(8), 1451-7
CODEN: JMCMAR; ISSN: 0022-2623

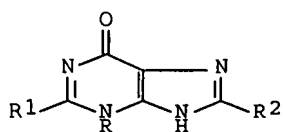
DOCUMENT TYPE: Journal

LANGUAGE: English

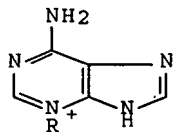
OTHER SOURCE(S): CASREACT 116:214213

ED Entered STN: 31 May 1992

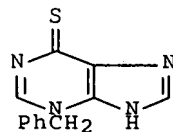
GI



I

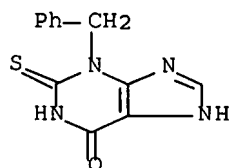
X⁻

II

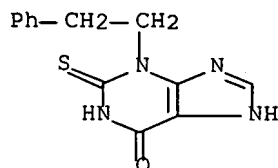


III

- AB 3-Substituted hypoxanthines I (R = CH₂Ph, CH₂C₆H₃Cl₂-3,4, CH₂C₆H₄CN-4, CH₂C₆H₄NO₂-4, CH₂C₆H₄OMe-4, CH₂CH₂Ph, 2-thienylmethyl, 2-furylmethyl; R₁ = H, SMe, OH, NH₂; R₂ = H, NH₂, NHCHO) and analogs II (R = CH₂Ph, X = Cl; R = CH₂C₆H₄NO₂-4, X = Br) and III have been synthesized as inhibitors of purine nucleoside phosphorylase (PNP), which may conceivably act as T-cell-selective immunosuppressive agents with potential utility in autoimmune disorders such as rheumatoid arthritis, in organ transplantations, and in T-cell leukemias. The compds. were evaluated for their PNP activity by a radiochem. assay and also for their cytotoxic effects on a T-lymphoblastoid cell line (MOLT-4). Appropriate substitutions on 3-benzylhypoxanthine (I, R = CH₂Ph, R₁, R₂ = H) increase potency. Variation of the 3-aryl substituents of I (R = CH₂Ph, R₁, R₂ = H) failed to further increase potency. Replacement of the 6-oxygen function in I (R = CH₂Ph, R₁, R₂ = H) to give II or III resulted in little change in activity. Other variations resulted in decreased activity. I (R = CH₂Ph, 2-thienylmethyl, 2-furylmethyl, CH₂C₆H₄OMe-4, R₁, R₂ = NH₂) have moderate but significant activities, as compared to the most active inhibitor presently known, 8-amino-9-thienylguanine. I (R₁, R₂ = NH₂) represent a novel structural type which were prepared via formation of the aminoimidazole moiety through a base-catalyzed 1,5-(O → N)-carbamimidoyl rearrangement.
- IT 28741-76-6P 139460-82-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation, reductive dethiolation, and purine nucleoside
 phosphorylase-inhibiting activity of)
- RN 28741-76-6 CAPLUS
- CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(phenylmethyl)-2-thioxo- (9CI) (CA
 INDEX NAME)



- RN 139460-82-5 CAPLUS
- CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(2-phenylethyl)-2-thioxo- (9CI) (CA
 INDEX NAME)



- L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
- ACCESSION NUMBER: 1976:105543 CAPLUS Full-text
- DOCUMENT NUMBER: 84:105543
- TITLE: Thermal decomposition of quaternary hypoxanthinium

Search #2 Claim 8 & some claim 9 species

salts and related purines

AUTHOR(S): Bergmann, Felix; Rahat, Miriam
 CORPORATE SOURCE: Hadassah Med. Sch., Hebrew Univ., Jerusalem, Israel
 SOURCE: Journal of the Chemical Society, Perkin Transactions
 1: Organic and Bio-Organic Chemistry (1972-1999)
 (1976), (2), 239-43
 CODEN: JCPRB4; ISSN: 0300-922X

DOCUMENT TYPE: Journal
 LANGUAGE: English

ED Entered STN: 12 May 1984

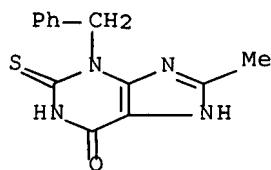
GI For diagram(s), see printed CA Issue.

AB Addnl. data considered in abstracting and indexing are available from a source cited in the original document. Thermal decomposition of quaternary hypoxanthinium salts was achieved by heating their solns. in DMF. 1,3-Dialkylhypoxanthinium bromides or iodides lost the 3-substituent as alkyl halide, which then attacked the imidazole ring at N-7 or N-9. Thermolysis of the dioxotetrahydropurinium iodide I (R = H) involved either loss of the 3-Me group as MeI giving the dihydromethylpurinedione II (R = H), or removal of HI to give the corresponding betaine which was then methylated at N-9 to give the dioxotetrahydropurinium iodide I (R = Me). The latter compound in turn decomposed to give the dimethylpurinedione II (R = Me). Similarly, the dimethylhypoxanthinium iodide III (R = H) was degraded mainly by loss of MeI, giving IV (R = H) and small amts. of V (R = H). III (R = H) also lost HI to give the corresponding betaine, which methylated at N-1 to give III (R = Me). III (R = Me) again underwent thermolysis to give a mixture of IV (R = Me) and its 9-Me isomer.

IT 59311-65-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation, reduction, and NMR of)

RN 59311-65-8 CAPLUS

CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-8-methyl-3-(phenylmethyl)-2-thioxo-(9CI) (CA INDEX NAME)



L9 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1970:466537 CAPLUS Full-text

DOCUMENT NUMBER: 73:66537

TITLE: N .far. N alkyl and glycosyl migration of purines and pyrimidines. III. N .far. N alkyl and glycosyl migration of purine derivatives

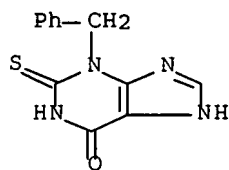
AUTHOR(S): Miyaki, Michiko; Shimizu, Bunji
 CORPORATE SOURCE: Cent. Res. Lab., Sankyo Co., Ltd., Tokyo, Japan
 SOURCE: Chemical & Pharmaceutical Bulletin (1970), 18(7), 1446-56
 CODEN: CPBTAL; ISSN: 0009-2363

DOCUMENT TYPE: Journal
 LANGUAGE: English

OTHER SOURCE(S): CASREACT 73:66537

Search #2 Claim 8 & some claim 9 species

ED Entered STN: 12 May 1984
AB Alkyl and glycosyl migration reactions of N1-, N3-, N7-, and N9-substituted derivs. of adenine, N6,N6-dimethyladenine, N2-acetylguanine, and purine were demonstrated. The NMR chemical shifts of these derivs. were determined and the frontier π -electron ds. of nitrogens in purine ring calculated by a simple LCAOMO method. The results provided the order of thermodynamic stability and kinetic effect of the derivs. on the alkylation reaction.
IT 28741-76-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 28741-76-6 CAPLUS
CN 6H-Purin-6-one, 1,2,3,7-tetrahydro-3-(phenylmethyl)-2-thioxo- (9CI) (CA INDEX NAME)

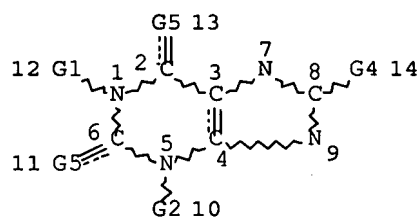


FILE 'HOME' ENTERED AT 16:17:29 ON 12 APR 2007

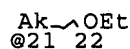
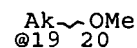
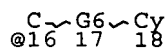
SEARCH HISTORY

=> d stat que l8; d his nofile

L1 STR



Ak @15



VAR G1=H/15

VAR G2=16/15/OME/OET/19/21

VAR G4=H/AK

VAR G5=O/S

REP G6=(0-5) C

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 15

CONNECT IS E2 RC AT 19

CONNECT IS E2 RC AT 21

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

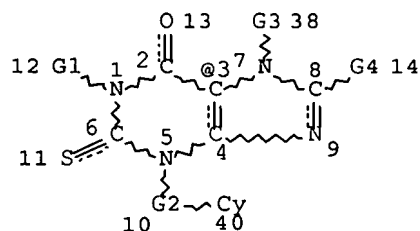
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NUMBER OF NODES IS 22

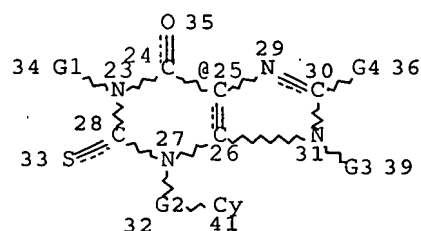
STEREO ATTRIBUTES: NONE

L4 17287 SEA FILE=REGISTRY SSS FUL L1

L5 STR



Ak @15



G10 37

VAR G1=H/15

REP G2=(1-6) C

VAR G3=H/15

VAR G4=H/15

VAR G10=3/25

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 15

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE

L8 17 SEA FILE=REGISTRY SUB=L4 SSS FUL L5

100.0% PROCESSED 229 ITERATIONS

17 ANSWERS

SEARCH TIME: 00.00.01

(FILE 'HOME' ENTERED AT 16:04:30 ON 12 APR 2007)

FILE 'REGISTRY' ENTERED AT 16:04:37 ON 12 APR 2007

L1 STR
 L2 50 SEA SSS SAM L1
 L3 115605 SEA SSS FUL L1 EXTEND
 L4 17287 SEA SSS FUL L1
 SAVE TEMP L4 BER537FULL/A
 L5 STR L1
 L6 1 SEA SUB=L4 SSS SAM L5
 D SCAN
 L7 229 SEA SUB=L4 SSS FUL L5 EXTEND
 L8 17 SEA SUB=L4 SSS FUL L5
 SAVE TEMP L8 BER537FULA/A

FILE 'REGISTRY' ENTERED AT 16:17:11 ON 12 APR 2007

D STAT QUE L8

FILE 'CAPLUS' ENTERED AT 16:17:15 ON 12 APR 2007

L9 8 SEA ABB=ON L8
 D IBIB ED ABS HITSTR 1-8

FILE 'HOME' ENTERED AT 16:17:29 ON 12 APR 2007

D STAT QUE L8

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